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STAGE OPERATIONS IN SEVERE HYPERTHYROIDISM

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AS THE result of our experience with 14,600 goiter operations, we have developed quite definite convictions concerning the fatalities which, though few, are inevitably associated with subtotal thyroidectomy in patients with severe degrees of hyperthyroidism.

While we cannot present indisputable evidence as to what are the effects of operative procedures upon the organism that brings about these deaths, we have repeatedly demonstrated that when we perform the operation of subtotal thyroidectomy in stages, the mortality rate is lowered, and that when we lessen the number of stage operations, the mortality rate rises. With this basic principle in mind, we have published and preached a formula relating to operations upon patients with serious hyperthyroidism which we believe is sound, and which will impel one to be conservative, and a plan which if consistently pursued will result in a lower mortality rate.

Our formula for low mortality rates has always been to assume that if a patient died after subtotal thyroidectomy, he would probably not have died had we performed a two stage subtotal thyroidectomy, after a right first stage subtotal hemithyroidectomy, sending the patient home for six weeks and then having him return for a second stage left subtotal hemithyroidectomy. Should a patient die after a right first stage hemithyroidectomy, we contend that patient would probably not have died after a preliminary pole ligation, and should a patient die after preliminary bilateral pole ligations, the patient would probably not have died had but one superior pole been ligated and the other pole ligated a week later.

The advent of preoperative preparation of patients with hyperthyroidism by the preliminary administration of iodine, usually in the form of Lugol's solution, has been a great advance in the management of these dangerous states. With it, however, have come certain unsound practices which, in some measure at least, have lessened the value of this great advance. One is the promiscuous employment of iodine without regard for the fact that iodine is of value in hyperthyroidism only in the preparation for operation, thus saturating them with iodine prematurely. Another is the tendency to assume that with the advent of the preoperative employment of Lugol's solution, pre-

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liminary pole ligations are no longer necessary. There can be no dispute but that the employment of iodine in the preparation of patients with hyperthyroidism for operation has lessened the number of stage operations, but in spite of this and all other advances in the methods of preparing these patients, there remains, as stated above, an apparently inevitable mortality. As long as this mortality exists there will be a need for graded operative procedures, and while we have never succeeded in eliminating mortality completely for any given year, we feel sure that our low mortality rates in primary hyperthyroidism are definitely related to the employment of graded procedures in patients seriously ill.

TABLE I

OPERATIVE MORTALITY AFTER MULTIPLE PROCEDURES UPON CASES OF PRIMARY AND SECONDARY HYPERTHYROIDISM

Ten Year Period, 1926–1935, Inclusive
5,626 *Operations*

	Per Cent of Patients with Multiple Operations	Operative Mortality
Primary hyperthyroidism	28.9	.48
Secondary hyperthyroidism	17.8	1.55

While the mortality of secondary hyperthyroidism has always been higher than that of primary, one cannot help but deduce from these figures that we have not performed enough multiple stage procedures in this type of hyperthyroidism.

In a recent article[1] dealing with our experience with pole ligation, we stated that it was an almost impossible undertaking to set down in words a description of the features of a case of hyperthyroidism which may be done in one stage, in two stages or one that should be preceded by preliminary pole ligation. Since the decision as to the type of operative procedure to apply to

TABLE II

THE POSTOPERATIVE EFFECT ON WEIGHT IN FIFTY PATIENTS WITH PRELIMINARY POLE LIGATION

Weight gain in 32 patients	64%
Weight loss in 14 patients	28%
No change of weight in 4 patients	8%

a given case is so difficult to make, it is obviously impossible to standardize the problem by dividing the patients into these groups.

TABLE III

THE EFFECT ON PULSE IN FIFTY PATIENTS WITH PRELIMINARY POLE LIGATION

Decrease in 31 patients	62%
Increase in 17 patients	34%
No change in 2 patients	4%

We offer that evidence that the employment of incomplete procedures produce at least temporary improvement in these cases and will discuss the

features which in our experience has convinced us they are serious risks. The problem of multiple stage procedures then concerns itself almost entirely with estimations of the severity of intoxication.

TABLE IV

THE EFFECT ON BASAL METABOLISM IN FIFTY PATIENTS WITH PRELIMINARY POLE LIGATION

Decrease in 33 patients	66%
Increase in 14 patients	28%
No change in 3 patients	6%

TABLE V

GAIN IN WEIGHT BETWEEN FIRST AND SECOND STAGES HEMITHYROIDECTOMY TWO HUNDRED FIFTY CASES

	Primary Hyperthyroidism 149 Cases	Secondary Hyperthyroidism 101 Cases	Total Two Stages
Gain in weight	86.5%	74%	82 %
Loss of weight*			14.8%
No change			3.2%

* All show drop in pulse rate and drop in metabolism.

TABLE VI

PULSE RATE CHANGE BETWEEN FIRST AND SECOND STAGES HEMITHYROIDECTOMY TWO HUNDRED FIFTY CASES

	Primary Hyperthyroidism 149 Cases	Secondary Hyperthyroidism 101 Cases	Total Two Stages
Pulse rate drop	80%	64%	73.2%
Pulse rate unchanged			24.4%
Pulse rate increased			2.4%

TABLE VII

BASAL METABOLISM CHANGE BETWEEN FIRST AND SECOND STAGES HEMITHYROIDECTOMY TWO HUNDRED FIFTY CASES

	Primary Hyperthyroidism 149 Cases	Secondary Hyperthyroidism 101 Cases	Total Two Stages
Drop in metabolism	90%	76%	84.8%
Unchanged			13.2%
Increased			2 %

It will always be true that of the small number of patients with hyperthyroidism dying in our Clinic each year postoperatively, some will be the result of cardiac complications, some will be the result of pulmonary com-

TABLE VIII

HIPPURIC ACID LIVER FUNCTION TEST IN HYPERTHYROIDISM*

Case	Age	Sex	Dur. of Disease	Wt. Loss	Basal Rate		Hippuric Acid Determination†			Clinical Diagnosis	Operative Procedure
					On Adm.	On 6th Day	On Adm.	Preop.	6 Days P. O.		
1	31	F	18 mos.	None	+81	+55	1.41	2.93	2.12	Primary Hyperthyroidism	Hemithyroidectomy
2	36	F	6 mos.	17 lbs.	+44	+38	1.72	2.26	1.82	P. H.	Hemithyroidectomy
3	27	F	2 yrs.	None	+76	+51	2.31	2.79	2.05	P. H.	Hemithyroidectomy
4	32	F	10 mos.	35 lbs.	+47	+30	1.52	1.72	2.09	P. H.	Hemithyroidectomy
5	37	F	2 yrs.	30 lbs.	+41	+31	2.22	—	2.65	P. H.	Subtotal Thyroidectomy
6	53	F	4 mos.	12 lbs.	+51	+28	1.93	2.51	—	Ad. Goiter with Hyperthyroidism	Subtotal Thyroidectomy
7	39	F	1 yr.	12 lbs.	+ 7	+17	2.83	2.94	—	P. H.	Subtotal Thyroidectomy
8	32	F	5 mos.	19 lbs.	+26	+16	2.45	2.88	2.58	P. H.	Subtotal Thyroidectomy
9	30	F	2 mos.	20 lbs.	+49	+21	2.16	2.84	2.55	P. H.	Subtotal Thyroidectomy
10	22	F	2 mos.	None	+18	+ 7	2.62	3.20	2.28	P. H.	Subtotal Thyroidectomy

* Unpublished Work of E. C. Bartels (Medical Dept. Lahey Clinic).

† Normal Hippuric Acid Secretion, Three Grams.

Constructed by Doctor Bartels, shows the possible depression of liver function as suggested by hippuric acid determinations, its elevation after several days of preoperative hospital preparation and its tendency to fall, perhaps due to the postoperative thyroid reaction, when determined six days after operation.

Further investigations are being carried on relative to late postoperative hippuric acid determinations, taken when these patients have attained normal postoperative metabolic levels.

plications, a trivial percentage will be the result of operative complications and the remainder will be the result of serious thyroid reactions. The first three states are perhaps in some measure influenced by multiple stage procedures, but the last state, postoperative thyroid reactions, is undoubtedly more definitely influenced by multiple stage procedures than any or all of the other three, and because of this, it becomes extremely important to consider the factors, when present, which indicate a severe grade of hyperthyroidism. These factors are divisible into those to be appreciated before the operation and those to be interpreted as indications of danger during operation.

If it be accepted that with hyperthyroidism there is quite constantly associated an increase in basal metabolism, and there are but very few today who fail to accept this assumption, then it must be accepted that hyperthyroidism is largely a disease of excessive combustion. Recent researches in liver function tests with hippuric acid undertaken in our Medical Department by Dr. E. C. Bartels corroborate what we and many others have long suspected, that hyperthyroidism lowers liver function and improvement from hyperthyroidism reelevates liver function.

TABLE IX

SPECIFICITY OF HIPPURIC ACID TESTS FOR LIVER FUNCTION IN PATIENTS SUSPECTED OF HYPERTHYROIDISM

Case	Age	Sex	Clinical Impression*	B.M.R.	Hippuric Acid
1	40	F	Primary Hyperthyroidism in Partial Remission	−12 −10	3.08
2	32	F	Primary Hyperthyroidism Gland Not Typical	± 0 − 7	3.00
3	44	F	Adenomatous Goiter with Questionable Thyroidism	+10	3.14
4	42	F	Adenomatous Goiter with Hyperthyroidism	+10 + 6	3.66
5	33	F	Mildly Toxic Adenomatous Goiter	+ 5	3.26
6	43	F	Adenomatous Goiter with Questionable Recurrent Hyperthyroidism	+14 +15	3.33
7	47	M		+12	3.23

* Prior to hospital study.

It is of interest to note that in these seven patients, all of whom were suspected of hyperthyroidism but upon hospital study proved not to have it, the hippuric acid determinations were normal.

That thyroid intoxication is the result of excessive thyroid secretion may be assumed, purely by deduction, since adequate subtotal thyroidectomy results in complete and permanent relief from this intoxication. The degree of damage from this intoxication may be estimated by both direct and indirect evidences. Of the direct evidences, the most definite and dependable, in adults particularly, is tachycardia. The next and but slightly less dependable is weight loss, and the least dependable evidence of severity of intoxication is basal metabolism. The indirect evidences, not of the intensity

of the intoxication entirely, but rather of the danger of operative fatality, are associated with the age of the patient, and so his or her ability to withstand the effects of excessive energy production and the length of time over which the effects of excessive energy production have been affecting the organism. During the period of preoperative preparation, valuable indirect evidence becomes available also as to what degree the actual excessive production of energy is resistent to its influence by iodine medication and to what degree its effects are counterbalanced by rest and a diet aimed toward overcoming weight loss and possibly restoring liver glycogen.

Tachycardia, although occasionally inconsistent, is, I believe, the best single evidence of the degree of hyperthyroidism. Patients who run persistently high pulse rates fall definitely into the bad risk group. I have a great many times, in writing on this subject, urged that when patients with hyperthyroidism are seen for the first time, a notation be made on the record as to the examiner's opinion of the severity of the disease, the probable need of a multiple stage procedure and the probable type of operation that will be needed. If this is done the tachycardia at the time of the first examination will be at its highest. Likewise, the patient's activation will be at its worst and if a prophecy as to the probable need of multiple stage procedures be recorded at this time, it will consistently be on the side of safety. If on the other hand, such a patient be seen in the Clinic and no note made as to the severity of the disease and need for stage procedures and a decision as to these stage procedures reached the day before operation, after the patient has had a week's rest in bed, and a large fluid, glucose and iodine intake, then one may forget that but a week previously that patient was thought to be a very bad risk patient. After this week's period of preparation the tachycardia may have markedly lessened, the basal rate dropped and the weight risen. Such deceptive observations tend to lead one into performing a one stage thyroidectomy that may result in a fatality. The decision at the operating table for or against a two stage hemithyroidectomy or a preliminary pole ligation will occasionally be easy, but in many more cases it will be an extremely difficult one and not infrequently based upon features that are far from convincing in either direction. In such a situation of uncertainty a record of one's impression of the severity of the disease and need for stage procedures made at the patient's worst when first seen will be of great value in helping to make this difficult and dangerous decision.

One can, I believe, more safely generalize about high trends of tachycardia than about low pulse rates. Severe and dangerous hyperthyroidism can exist in the presence of such relatively low pulse rates as 110, 120 or 130, but persistent pulse rates of 150 and upward are certain evidence of severe hyperthyroidism and a warning that should make one correlate this danger indicating factor with other danger signals to be spoken of later, and seriously consider and determine as to whether or not a multiple stage procedure should be done.

Weight loss of considerable amount, 30, 40, 50 or more pounds, provided, of course, that the patient has not been on a restricted diet, is definite evidence that the excessive production of energy has resulted in the patient burning a fraction of himself and suggests strongly the need for multiple stage measures. If one wishes to keep the mortality of subtotal thyroidectomy for hyperthyroidism low, it will not suffice to employ multiple stage procedures in patients only who are so ill with hyperthyroidism that stage operations must obviously be done. There is a large group of borderline cases in whom unexpected postoperative reactions will occur and occasionally result in fatalities. In many patients, multiple stage operations must be performed on the suspicion that a serious postoperative thyroid reaction might occur. It is, therefore, wise to accept a large weight loss as evidence of the severity of the intoxication even though other evidences may be lacking. Likewise, as indirect evidence, one must accept the probability that those patients who have had hyperthyroidism for a long time have perhaps suffered considerable liver damage and at any rate are often more capable of having a severe postoperative reaction than the patient who has had hyperthyroidism but a short time.

There seems little question but that age plays a great part in the mortality associated with any trying operative ordeal which an individual has to withstand. For example, the mortality rate in our patients below 50 years having subtotal gastrectomy is practically half that of patients over 50 years having this operation. Similar influences are effective in elderly patients with severe degrees of hyperthyroidism. We have always been impressed with the fact that young individuals, even when in quite severe states of hyperthyroidism, could and would withstand complete subtotal thyroidectomies much better than older individuals in much less severe states of thyroid intoxication.

Should the question of possible multiple stage procedures arise and still not be capable of settlement on the information already discussed, then one should make use of the indirect evidence available in order to arrive at such a decision. If during the period of hospital preparation there has been a slight weight loss or no weight gain in spite of a high caloric diet, if the basal metabolism and pulse rate have risen or have even not diminished, in such a case under discussion as to possible multiple stage procedure, the decision should be in favor of them.

Multiple stage procedures should, I feel, always be considered in all patients who have recently had vomiting or diarrhea or any of the signs of a thyroid crisis. This procedure will also at times be necessary in thyrocardiacs with advanced degrees of decompensation and associated high degrees of hyperthyroidism.

Not infrequently, in spite of the above stated facts, one will still be uncertain as to whether or not patients will safely endure a complete subtotal thyroidectomy or will need a two stage right and left subtotal thyroidectomy.

Then the decision as to whether or not but one-half of the operation should be performed must be left until one-half of the operation is completed. The operation is interrupted at this point, the history and findings reread and certain things in the course of the operation up to this point reviewed and their significance evaluated as an aid in settling as to whether or not to go on with a left subtotal hemithyroidectomy. When one is in doubt in reviewing such a situation, some of the facts which should influence one in favor of multiple stage measures are here submitted: A progressively rising pulse rate, an increasingly widening pulse pressure (perhaps the best blood pressure indication of dangerous toxicity), a high demand for anesthesia depth and a demand for unusually high percentage of oxygen, the fact that any technical difficulties have been encountered such as an excessive amount of bleeding, the employment of an unusual amount of time to complete the hemithyroidectomy or any technical complication which has rendered the operation unduly difficult. In this respect, it must be remembered that if difficulties have been encountered, in right subtotal hemithyroidectomy they may quite likely be encountered on the other side and so the doubtful risk patient committed to a predictable hazard which is more than usual.

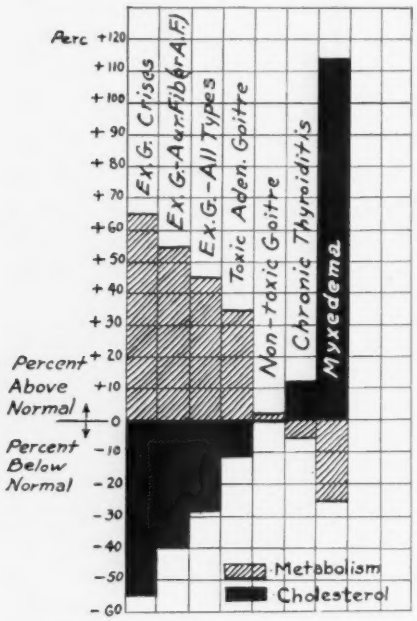

CHART 1.—The correlation of hypocholesterolemia with the grades of hyperthyroidism and that of hypercholesterolemia with the grades of hypothyroidism is shown by Dr. L. M. Hurxthal in previous reports from this Clinic.

Because we constantly have so many patients in severe degrees of thyroid intoxication, the problem of deciding for or against multiple stage measures is a daily one and one that often has to be settled several times each day. While one does not routinely have either blood iodine or blood cholesterol reports on every case, it is possible in cases under consideration for multiple stage operations to have either or both of these reports and they provide additional data to be utilized in making these difficult decisions.

Dr. L. M. Hurxthal has published the results of his investigations in this Clinic on blood cholesterol in thyroid states in several articles on this subject. It has been convincingly demonstrated by him that there is a high blood cholesterol with hypothyroidism and a low blood cholesterol with hyperthyroidism. It has further been demonstrated by him that the degree of hypocholesterolemia relates itself to the degree of hyperthyroidism, and likewise, that the degree of hypercholesterolemia relates itself to the degree of hypothyroidism.

In a recent further investigation on this subject, Doctor Hurxthal has concluded that high blood cholesterol is the result of the inability of the hypothyroid patient to metabolize cholesterol and that the low blood cholesterol in the hyperthyroid patient is due to excessive destruction or utilization of cholesterol. Very low blood cholesterol, therefore, must be accepted at least as presumptive evidence of a severe grade of hyperthyroidism. Unfortunately, the range of abnormal blood cholesterol in the downward direction is so great, 120 being low normal and 70 the lowest hypocholesterolemia we have seen with hyperthyroidism, that as an indicator of a possible serious postoperative reaction it is not as valuable a factor as we would like it to be.

During the last two years, Mr. H. J. Perkin has been carrying on investigations in the Clinic on the relation of blood iodine to hyperthyroidism, and has demonstrated that in a majority of patients having hyperthyroidism, there is an elevation of the blood iodine. Preoperatively out of a group of 331 patients with hyperthyroidism, 224 or about 70 per cent had an elevation of blood iodine. Following relief from hyperthyroidism by subtotal thyroidectomy, the elevation in blood iodine in this group promptly dropped to normal in direct proportion to the drop in basal metabolism. Of these 331 cases of hyperthyroidism, however, 107 or about 30 per cent had a normal preoperative blood iodine which rose to above normal after operation, and later with the drop in the metabolism to normal again returned to normal. This is an interesting and somewhat confusing phenomenon from the point of view as to whether or not blood iodine represents the iodine fraction of circulating thyroxine. Of direct interest to us, however, in our search for every indication of severity of intoxication in patients with hyperthyroidism is the fact that in the 70 per cent of patients having blood iodines which were elevated preoperatively (224) multiple stage operations were performed on 38 patients (17.9 per cent), while of the 107 (30 per cent) patients with hyperthyroidism having normal blood iodines preoperatively, multiple stage procedures were performed in 49 cases (45.8 per cent). When one realizes that the grading of risks and selections of a multiple stage procedure in those cases were made without reference to, or knowledge of, what the blood iodine values were and when one appreciates that the average percentage of multiple stage procedures in our entire group of patients with hyperthyroidism is almost 22 per cent, then one must seriously consider the possibility that low blood iodines are an indication of a severe grade of hyperthyroidism and one in which multiple stage procedures must be considered and will probably need to be employed in a higher percentage of cases than in those patients with high blood iodines. If one realizes also that in this group of patients with low preoperative blood iodines, there is a higher percentage of recurrent hyperthyroidism than in the average group, this becomes additional evidence that low preoperative blood iodines in patients with definite hyperthyroidism are probably an indication of severity of the disease.

TABLE X

STAGE OPERATIONS IN RELATION TO THE PREOPERATIVE BLOOD IODINE LEVEL

	Elevated Blood Iodine	Normal Blood Iodine
No. of Cases	224 (70%)	107 (30%)
Stage Oper.	38	49
% of group	17.9	45.8

Note that in the 70 per cent of patients having high preoperative blood iodine but 17.9 per cent had multiple stage operations, but that in the 20 per cent having low preoperative blood iodine 45.8 per cent had multiple stage procedures.

SUMMARY

Since the necessity for and the percentage of multiple stage operations should, we believe, be directly related to the severity of the hyperthyroidism, we have discussed the direct and indirect evidences of hyperthyroidism with the possible relation of atypically low preoperative blood iodines as indications of a severe degree of thyroid intoxication.

REFERENCE

[1] Lahey, Frank H., and Schwalm, L. J.: Pole Ligation in the Treatment of Hyperthyroidism. Surg., Gynec., and Obstet., **63**, 69–76, July, 1936.

HYPERPARATHYROIDISM IN SIBLINGS

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VON RECKLINGHAUSEN first recognized generalized osteitis fibrosa cystica as an entity in 1891, but its etiology was not determined until much later. So many comprehensive reviews of the clinical, metabolic, pathologic and surgical aspects of hyperparathyroidism have appeared in the literature that it is not within the scope of this report to elaborate in detail upon these points. The main features of this disturbance, however, will be illustrated in the case reports of two members of the same family. The bony lesions of these two patients, brother and sister, were first diagnosed erroneously—roentgenologically in one case and pathologically in the other—as giant cell tumors. Later both patients were successfully treated for hyperparathyroidism associated with generalized osteitis fibrosa cystica, by the surgical removal of parathyroid adenomata. Though this disease is not considered to be of a familial nature, these cases illustrate that it may occur in more than one member of the same family and must be differentiated, therefore, from fragilitas ossium and similar familial skeletal disturbances.

CASE REPORTS

Case 1.—An Italian girl, age 17, entered the University of California Hospital January 18, 1934. One year previously she had injured her left shoulder and sustained a pathologic fracture of the neck of the left humerus. She had had no complaints prior to that time. A roentgenologic diagnosis of giant cell tumor was made, the region was immobilized and a course of roentgen therapy instituted. She felt improved for a short time, but later noticed the insidious development of polydipsia, polyuria, constipation, increased fatigability, severe attacks of left ureteral colic, and pain in the left humerus and right tibia. At this time she was seen by Dr. Harold Brunn, who referred her to the University of California Hospital.

Physical examination revealed a girl of short stature, with a waddling gait. She was well developed and her skeletal musculature showed no clinical signs of hypotonicity, although prolonged exertion caused fatigue. Her teeth were in good condition. There was a visible, palpable tumor, apparently located in the left lobe of the thyroid gland. Limitation of motion and swelling of the left shoulder joint were present, as well as tenderness over the left humerus, right tibia, and left kidney.

TABLE I

DAILY AVERAGE EXCRETION OF CALCIUM AND PHOSPHORUS IN CASE 1

	Case 1. 24-hour Average					
	Stool	Urine	Total	Intake	Balance	Blood
Calcium	0.1440	0.3727	0.5167	0.929	−0.4238	19.20 mg. per cent
Phosphorus	0.1703	0.7027	0.8730	0.7766	−0.0964	2.56 mg. per cent
Phosphatase						33.2 units

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The serum calcium level was elevated to 19.2 mg., and the plasma phosphatase to 33.2 (Kay-Jenner) units per 100 cc. of blood; the serum phosphorus was lowered to 2.5 mg. A study of the balance of the intake and output of calcium, by Aub's method,[1] revealed a markedly negative calcium balance. On a daily intake of 0.929 Gm. of calcium, the loss was 0.5167 Gm., or a negative balance of 0.4238 Gm. in 24 hours, 75 per cent of which was excreted in the urine (Table I). The urine was cloudy, yellow, acid

FIG. 1.—Roentgenogram showing marked thinning of the cortex and demineralization of the humerus; there is a cyst of the humeral head.

FIG. 2.—Roentgenograms of the right tibia showing a large cyst. (A) Before operation. (B) Thirteen months after the removal of the parathyroid adenoma.

in reaction, and had a specific gravity of 1.022. The test for sugar was negative and there was the faintest possible trace of albumin. From 20 to 25 red blood cells per high dry field were found in the uncentrifuged specimen. The intramuscular phenolsulphonephthalein test showed an excretion of 55 per cent of the dye after two hours. Examination of the blood showed a hemoglobin of 80 per cent, red blood cells 4,230,000, white blood cells 7,870, with 75 per cent polymorphonuclear neutrophils, 1 per cent eosinophils, 8 per cent large lymphocytes, 13 per cent small lymphocytes, and 3 per cent monocytes.

The bleeding time was 1.5 minutes (Duke) and the clotting time was five minutes (Lee and White). The tests of blood chemistry showed a fasting blood sugar level of 103.4 mg., non-protein nitrogen 52.1 mg., cholesterol 217.9 mg., serum albumin 4.69 Gm., serum globulin 2.19 Gm., and total protein 6.83 Gm. per 100 cc. of blood. The blood Wassermann and Kahn tests were negative. The basal metabolic rate was plus 1. Serial electrocardiograms showed a shortened Q-T interval (electric systole), delayed auriculo-ventricular conduction and slurred ventricular complexes, indicating hypotonicity of the cardiac musculature.[2]

FIG. 3.—(A) Parathyroid adenoma within the capsule of the left lobe of the thyroid gland. (B) Cut section of the adenoma, showing cystic degeneration. (C) Gross appearance of the adenoma after enucleation (Case 1).

Roentgenograms revealed generalized demineralization of the entire skeleton, characterized by a uniform granular osteoporosis. Cysts of varying sizes, some with cortical expansion, were present in the humeri (Fig. 1), right tibia (Fig. 2), metacarpal and pubic bones. The trabeculae of the long bones were indistinct and the cortex was thinned. Granular mottling was noted in the skull. The renal shadows were denser than normal and several small calculi were present in the left kidney. Gastro-intestinal roentgenologic series revealed a 40 per cent retention of barium in the stomach after six hours, suggesting hypotonicity of the gastro-intestinal musculature.

After exploring the retrotracheal and retro-esophageal planes of the neck, as well as

palpating the anterior and posterior mediastinum, a parathyroid adenoma, weighing 11.8 Gm. and measuring 3.7 by 2.8 by 3 cm., was removed from within the capsule of the left lobe of the thyroid gland at its inferior pole (Fig. 3). The right lobe appeared to be normal. A normal right inferior parathyroid gland was seen attached to the posterior capsule. The adenoma was inclosed in a smooth capsule, and the cut section revealed a characteristic yellowish-brown surface with a cystic center. The tissue was soft and glistening. The capsule was partially surrounded by a thin rim of normal parathyroid tissue. Microscopic sections showed the tissue to be composed of diffuse sheets or columns of epithelial cells, the majority of which were large, with eccentrically placed hyperchromatic nuclei and abundant clear cytoplasm, conforming to the *wasserhelle* or water-clear type of cell as described by Mallory and Castleman.[6] Some areas showed a pattern with a basal arrangement of the nuclei suggesting a pseudoglandular formation. There were also many groups of typical chief cells of smaller size, and transitional *wasser-*

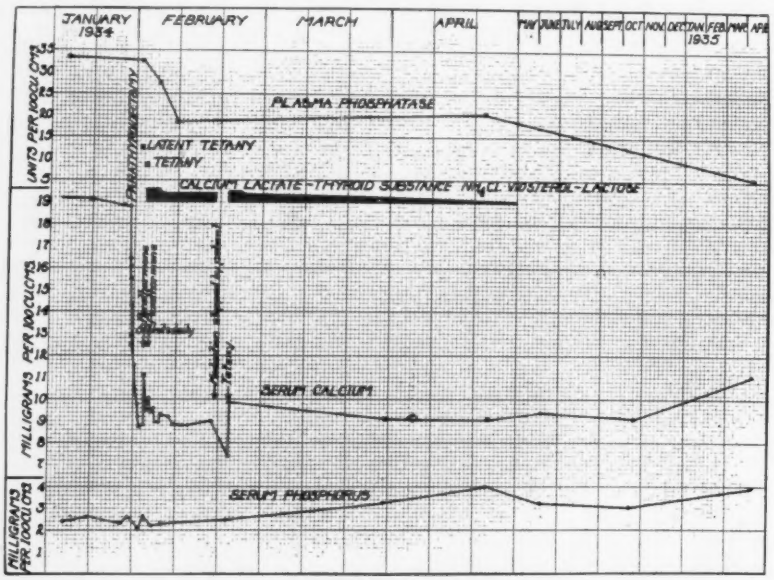

CHART I.—Showing the changes in the levels of serum calcium and phosphorus, and plasma phosphatase following the removal of the parathyroid adenoma (Case 1).

helle cells. Rarely a small group of light oxyphil cells could be seen. These cellular elements were supported by a stroma of fine fibrous tissue.

On the second day after operation, with a serum calcium level of 10.2 mg., the patient developed latent tetany and, on the morning of the third day, with a serum calcium level of 8.8 mg., she had spontaneous parathyroid tetany (Chart 1), characterized by carpopedal spasms, numbness, and paresthesias. Treatment with parathormone, calcium lactate, thyroid substance, ammonium chloride, lactose, and viosterol brought the calcium and phosphorus in the blood to a normal level. The pain and tenderness in the bones disappeared within three days after operation. The patient developed a positive calcium balance, with normal levels of calcium, phosphorus, and phosphatase in the blood; she no longer had pain and tenderness in the bones, hematuria or ureteral colic. Roentgenologically the skeleton showed increased calcification or complete obliteration of the cysts, 13 months after the removal of the parathyroid adenoma. The electrocardiogram revealed that the shortened Q-T interval had become prolonged and the other abnormal findings had reverted toward the normal. There was no retention of barium in the stomach after six hours. Both of these findings suggest a change from a state of muscu-

lar hypotonicity toward normal. At the last examination, she had no symptoms except some limitation of motion of the left shoulder joint resulting from the cystic formation and pathologic fracture.

Case 2.—After the first patient was studied, it was discovered that her brother, age 23, was being treated for a giant cell tumor of the mandible. At this time eight other members of the family were examined, but no clinical or metabolic evidence of skeletal or renal disease was found. Seven months before we saw this second patient, he had noted a painful swelling of the symphysis of the mandible and later sustained a pathologic fracture. A biopsy revealed a giant cell reaction which was interpreted as being indicative of a giant cell tumor. The patient was given a course of roentgen therapy, without improvement. He then developed general malaise and easy fatigability but had no pains in other parts of his skeleton and no urinary symptoms. Because of his sister's improvement, he came to the hospital for further investigation.

Physical examination revealed a well developed man of short stature, with a tender swelling of the mandible and a small palpable nodule in the left lobe of the thyroid gland. His teeth were sound. There was no clinical evidence of hypotonicity of his skeletal musculature or tenderness over his bones. The remainder of his examination was negative.

The serum calcium was elevated to 17.5 mg., the plasma phosphatase to 10.3 units (Kay-Jenner) per 100 cc. of blood, and the serum phosphorus was lowered to 1.5 mg. There was a markedly negative calcium balance. On a daily intake of 0.1040 Gm. of calcium, the loss was 0.3782 Gm., or a negative balance of 0.2742 Gm. in 24 hours, 80 per cent of the excretion being in the urine (Table II). Urinalysis revealed clear, yellow,

TABLE II

DAILY AVERAGE EXCRETION OF CALCIUM AND PHOSPHORUS IN CASE 2

	Case 2. 24-hour Average					
	Stool	Urine	Total	Intake	Balance	Blood
Calcium	0.0480	0.4302	0.4782	0.1040	−0.3742	18.20 mg. per cent
Phosphorus	0.2801	0.7676	1.0477	0.8480	−0.1997	2.10 mg. per cent
Phosphatase						10.3 units

neutral urine, without albumin or sugar. The centrifuged specimen showed a rare hyaline cast and 10 pus cells per high dry field. No red blood cells were found. Examination of the blood showed the hemoglobin to be 90 per cent, red blood cells 4,300,000 and white blood cells 4,150, with 60 per cent polymorphonuclear neutrophils, 26 per cent lymphocytes, 4 per cent eosinophils, and 14 per cent monocytes. The blood sugar estimation was .068 mg., and the non-protein nitrogen was 30.6 mg. per 100 cc. of blood. The blood Wassermann and Kahn tests showed a four plus reaction. The basal metabolic rate was minus 23. The kidneys excreted 35 per cent of the phenolsulphonephthalein after two hours. The Q-T interval of the electrocardiogram was shortened.

Roentgenograms revealed generalized changes characteristic of primary hyperparathyroidism. A generalized demineralization of the skeleton was noticeable, with findings similar to those in Case 1. This patient had only one cyst of the symphysis of the mandible (Fig. 4) and a small cyst in one of the phalanges. There were no renal calculi present. Roentgenograms of the esophagus showed a notched deviation to the right just below the level of the larynx (Fig. 5). Otherwise the gastro-intestinal series was negative.

An adenoma of the left inferior parathyroid gland, weighing 6.5 Gm. and measuring 3 by 2 by 2 cm., was removed from a retrotracheal position on the same plane as the esophagus (Fig. 6). The palpable nodule in the left lobe proved to be a small adenoma of the thyroid gland. The gross appearance of the parathyroid adenoma was charac-

FIG. 4.—Roentgenogram showing a cyst of the mandible with a pathologic fracture (Case 2).

FIG. 5.—Roentgenogram showing the deflection of the esophagus by a retrotracheal parathyroid adenoma (Case 2).

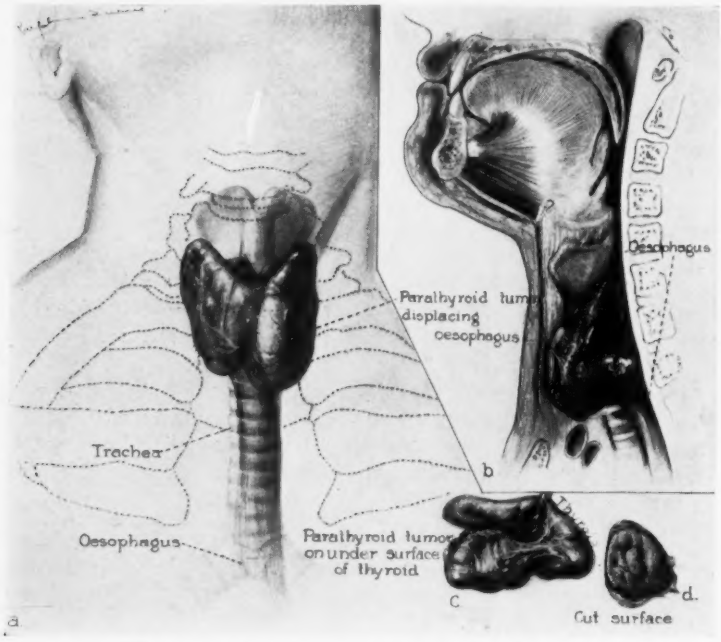

FIG. 6.—The position of the parathyroid adenoma in Case 2; (a) Anteroposterior view, showing the deflection of the esophagus to the right. (b) Left lateral view demonstrating the retrotracheal position of the adenoma. (c) Comparative sizes of the adenoma and the left lobe of the thyroid gland. (d) Cut surface of the adenoma.

teristic and it had a thin rim of compressed normal parathyroid tissue on its border. Microscopically, it was composed mainly of chief cells with numerous large groups of pale oxyphil cells. No *wasserhelle* cells were seen.

No signs of tetany developed, and the blood chemistry returned to normal (Table III and Chart 2). Fourteen months after operation, the patient was entirely free from

TABLE III

DAILY AVERAGE EXCRETION OF CALCIUM AND PHOSPHORUS IN CASE 2

HIGH CALCIUM, LOW PHOSPHORUS DIET
POSTOPERATIVE STUDIES

First period 4 days, 24-hour Average

	Stool	Urine	Total	Intake	Balance	Blood
Calcium*.....	0.5960	0.1922	0.7882	0.8570	+0.0688	16.99 to 9.34 mg. per cent
Phosphorus.....	0.1790	0.0643	0.2433	0.7160	+0.4727	1.93 to 2.74 mg. per cent

Second period 3 days, 24-hour Average

Calcium†.....	0.6933	0.0265	0.7198	1.5823	+0.8625	9.70 mg. per cent
Phosphorus.....	0.1433	0.3307	0.4740	1.2940	+0.8200	2.44 mg. per cent

* The first postoperative study was from March 19 to March 22, inclusive. There was no intake on March 19—the day of operation. No calcium was given other than in the diet. Aspirin and codeine were the only drugs administered.

† The second postoperative study was from March 23 to March 25, inclusive. No calcium was given other than that in the diet. Phenobarbital was the only drug administered.

symptoms, the cyst of the mandible was becoming calcified and smaller, and calcification of the demineralized skeleton was taking place. The shortened Q-T interval of the electrocardiogram became prolonged and his renal function improved. Fatigue, which

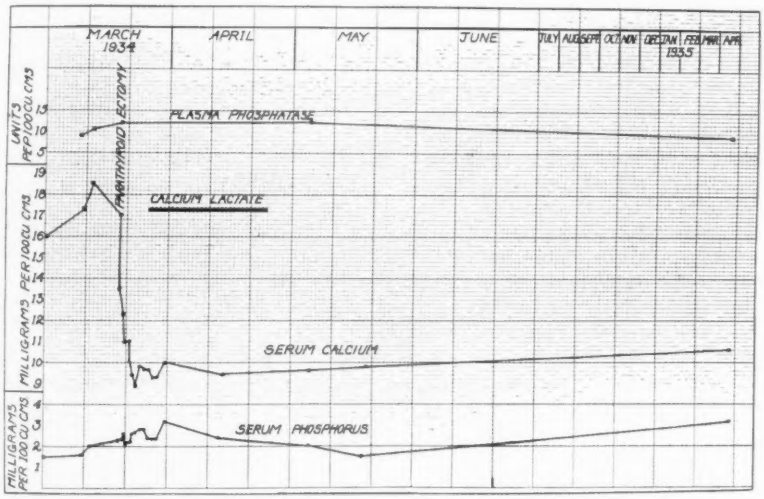

CHART 2.—Showing the changes in the levels of serum calcium and phosphorus, and plasma phosphatase following the removal of the parathyroid adenoma (Case 2).

had been an outstanding symptom, disappeared completely and the patient was able to perform manual labor.

COMMENT.—These two case reports illustrate the clinical, metabolic, and roentgenologic findings associated with the classic type of von Recklinghausen's disease. The levels of calcium and phosphorus in the blood were striking (Tables I and II). In both cases there was evident hypercalcemia. Conversely, the phosphorus was lower than normal. In the first case, the phosphatase was definitely elevated. In the second, it was not so obviously so, and we are inclined to correlate this with the lessened involvement of bone, inasmuch as the amount of phosphatase is an index of the activity of bony metabolism (destruction and repair).

One patient had renal calculi; the other did not. On the basis of the metabolism, one could not anticipate which patient would have kidney stones, since, in both instances, the excessive urinary loss of calcium and phosphorus would presumably favor the formation of such stones. Perhaps the extent of the process in the first patient would suggest a disturbance of metabolism of longer standing, which would favor lithiasis.

The postoperative studies in the second case are interesting (Table III), as we may observe the transition from the hypercalcemia of hyperparathyroidism to the hypocalcemia of hypoparathyroidism. Obviously, however, the tests were not comparable to those made before operation, since the intake of calcium was many times greater (for the 24 hour period) than in the preoperative test, so that there was a disproportion between the intake of calcium and that of phosphorus.

As Shelling and Goodman[3] have shown, it is important to meet the immediate reversal of function following parathyroidectomy by a diet low in phosphorus and high in calcium, which helps to guard against further depression of the calcium. While this is ordinarily accomplished by administration of calcium, we believe that a careful restriction of phosphorus is of additional benefit. Additional calcium was not given in the cases cited, as we desired a minimal intake in order to detect the endogenous (endocrine) factors.

This study illustrates remarkably well the shift of the excretion of calcium from urine to stool, and the change to a positive balance. That this is a temporary phenomenon must be admitted, since follow up subsequently has shown no persistent tetany and no hypocalcemia. We think it likely that a further study might show a readjustment to that of the normal adult metabolism.

In each of these two cases, an erroneous diagnosis of giant cell tumor was made, roentgenologically in one, and microscopically, after biopsy, in the other. There are certain differentiating points between giant cell tumor and the giant cell variant of osteitis fibrosa cystica. The former is usually situated asymmetrically at the epiphyses of the long bones; namely, the lower end of the radius and femur and the upper end of the tibia, and usually is single rather than multiple. The giant cell variant of osteitis fibrosa may occur in the shaft of the bone, subperiosteally or centrally, and is associated with generalized demineralization of the skeleton and altered calcium and phos-

phorus metabolism. This lesion is more likely to be multiple. Although there is some controversy concerning this differentiation by pathologic means, many contend that there is a difference in the stroma. If one includes a small portion of surrounding bone proper, in the biopsy, the histologic picture of osteitis fibrosa should be evident enough to suggest hyperparathyroidism in those cases of giant cell variant.

Both patients sought medical attention because of pathologic fractures. The patient with the more advanced demineralization of the skeleton, longer history, higher serum calcium level, and larger tumor, developed tetany after operation, while the other patient, having these characteristic findings in a lesser degree, did not develop signs of hypoparathyroidism. The first patient developed symptoms and signs of latent tetany on the second day after operation with a normal serum calcium level of 10.2 mg., indicating that a sudden drop in the amount of calcium in the serum may produce symptoms suggesting hypocalcemia in the same way that the sudden drop in blood sugar level may produce symptoms suggesting hypoglycemia in a patient with diabetes mellitus, even though the actual level is normal or above.

In each case, the symptoms and signs rapidly disappeared following the removal of the parathyroid tumors, and a deposition of minerals in the skeleton took place within a short time. A markedly negative calcium balance became positive after parathyroidectomy, indicating that reconstruction of the skeleton was taking place. In time, a normal negative balance may be expected to supersede this. The outstanding symptoms of easy fatigability underwent the most marked subjective improvement.

Discussion.—There are three important types of parathyroid hyperfunction (exclusive of that caused by malignant tumors): the adenomatous, the hyperplastic associated with renal calculus, and the secondary, compensatory hyperplastic type. Only in the first two is parathyroidectomy indicated.

In 1907, Erdheim,[4] by experimental and anatomic means, demonstrated the enlargement of all the parathyroid glands in osteomalacia. He concluded that this enlargement was of a secondary, compensatory nature—that is, a result, rather than a cause, of disease of the skeleton. It was found later that this secondary parathyroid hyperfunction was associated with other types of diseases of the skeleton, such as arthritis, osteitis deformans, multiple myeloma, metastatic carcinoma and rickets, as well as scleroderma and nephritis. We had the opportunity to study a young patient with renal rickets who, at autopsy, showed the same type of hyperplasia of all the parathyroid glands.[5]

In the consideration of hyperparathyroidism associated with generalized osteitis fibrosa cystica, a careful distinction must be made between this secondary, compensatory parathyroid hyperplasia and parathyroid adenoma. Parathyroid enlargement, with resulting hyperparathyroidism, may be either hyperplastic or adenomatous. Hyperplasia affects all the tissue, but an adenoma usually involves only one, or at most two, of the glands. It seems logical to assume that hyperplasia, therefore, is dependent upon an external

stimulant while an adenoma is the result of local factors caused by neoplastic growth.[6]

In 1925, Mandl[7] removed a large parathyroid adenoma from a patient who thereafter obtained marked clinical improvement in the skeletal symptoms and signs of generalized osteitis fibrosa cystica. Following the report of this operation, parathyroidectomy was performed for many of the previously named conditions, until it was established that generalized osteitis fibrosa cystica is the only one of these diseases caused by a parathyroid adenoma. Microscopically, Mallory and Castleman[6] differentiated hyperplasia from adenomatous enlargement. They found the chief cell, or one of its transition, to be the important constituent of the adenoma associated with hyperparathyroidism in the majority of cases.

Recently Albright[8] discovered several cases of hyperplasia of the parathyroid glands by obtaining routine serum calcium and phosphorus determinations on patients with renal calculi. Those patients who showed a high serum calcium and a low serum phosphorus, though they showed no skeletal changes or elevation of the plasma phosphatase, were operated upon and enlarged hyperplastic parathyroid glands of different sizes removed. These patients improved following the removal of the main bulk of their parathyroid tissue. They seem to fall into a separate group from the secondary hyperplasias mentioned above. We have not encountered such a case nor any reports of similar cases from other clinics.

One should be familiar not only with the anatomic regions encountered in the ordinary thyroidectomy but also with the appearance, aberrant locations, and difficulties in locating tumors of the parathyroid glands. Roentgenologic evidence of deviation of the trachea or esophagus may aid in locating the tumor before operation. Walton,[9] Churchill,[10] and Lahey[11] have emphasized the importance of being prepared to make a thorough search in the retrotracheal and retro-esophageal planes of the neck, the lateral triangles of the neck, and in the anterior and posterior mediastinum. To overlook the tumor at the first operation may rob the patient of a chance for cure, because of the great difficulty in exploring the neck and mediastinum subsequently through a firm bed of scar tissue. We feel that, if a tumor is not found, removal of a normal parathyroid gland is not only without therapeutic effect but may be harmful. Likewise, we are skeptical concerning the removal of normal glands for many conditions alleged to result from parathyroid hyperfunction.

CONCLUSIONS

(1) Primary hyperparathyroidism is a clinical entity caused by one or more parathyroid adenomata and has a definite train of clinical, metabolic and roentgenologic findings. The diagnosis is based on a study of these three factors and not on any one alone. Primary hyperparathyroidism should not be confused with secondary compensatory parathyroid hyperplasia.

(2) The two cases reported show that the presence of malacic disease

in two members of the same family does not necessarily point to a diagnosis of fragilitas ossium or to any other type of familial skeletal disturbance.

(3) When a diagnosis of giant cell tumor is made by pathologic or roentgenologic methods, metabolic studies should follow.

(4) A conservative attitude should be taken concerning the removal of normal or hyperplastic parathyroid glands for a multiplicity of conditions.

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CYCLOPROPANE ANESTHESIA IN THYROIDECTOMY*

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FROM 1919 to October 23, 1935, in a series of goiter operations well in excess of 4,000 cases, nitrous oxide and oxygen (with or without ether) had become the anesthetic of choice in the Goiter Clinic of the Long Island College Hospital. In general, the patients were kept well under control. The postoperative recovery was, as a rule, quite prompt. Postoperative crises and acidosis were, for the most part, adequately controlled. Complications referable to anesthesia per se were indeed few and our mortality rate had continued downward.[1]

Since October 23, 1935, we have, to a large extent, been using cyclopropane in goiter operations. Cyclopropane or trimethylene is a "ring" hydrocarbon first prepared by Freund in 1882. No use was made of the agent until 1929, since which time it has been finding increased application as an anesthetic of great value. An important experimental contribution appeared in 1934 from the University of Wisconsin.[2] Since this time cyclopropane has been found to be an extremely potent anesthetic with little evidence of immediate or delayed toxicity, if given in amounts not in excess of that necessary to produce surgical anesthesia. Cyclopropane, like ether, probably owes its anesthetic properties in part to its solubility in lipoids. It is inflammable and, like ether and ethylene, forms explosive mixtures with air and oxygen. Precautions are thus necessary.

Cyclopropane is said to have the potency of chloroform and ether without their irritant qualities and, except in very high concentrations, it is not measurably harmful to liver, kidneys or heart.[3] A very high potency is necessary to produce spasm of the larynx. The anesthetist must guard against crowding the patient from the induction stage to the deeper stages of narcosis, since the usual laryngeal reflexes are not present to warn him. Cyclopropane does not stimulate respiration. In contradistinction to nitrous oxide and ethylene which produce an initial increase in the rate and volume of respiration and even depression from oxygen insufficiency, cyclopropane usually causes little if any change in the rate and volume of breathing unless concentrations greatly in excess of 20 per cent are used. The large amount of oxygen given with the gas prevents cyanosis and the blood thus constantly maintains a bright crimson color. It has been stated that capillary bleeding is increased by cyclopropane. In a small series of cases, we determined the coagulation and bleeding times before and at the end of operation and found no appreciable deviations from the normal. Other factors may of course be concerned in this matter. The

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impression of an apparent increased bleeding is doubtless based on the surgeon's continued visualization of a bright crimson operative field, and the notion has probably no real foundation in fact.

The method of administration has been that of the carbon dioxide absorption technic in a closed circuit. Expired carbon dioxide is retained in the soda lime. The oxygen consumed is replaced by a constant measured flow of oxygen equal to, or in excess of, the patient's requirements. We have not changed the premedication. Amytal (one and a half grains) is given the night before operation. An hypodermic of morphine—⅛ to ⅙ of a grain—is given one hour before operation and repeated immediately before the patient is sent to the operating room. Too much preliminary medication tending to depress respiration is not advisable since cyclopropane is not a respiratory stimulant.

Only a few minutes are required to produce anesthesia with cyclopropane in the average patient with hyperthyroidism. Unusually nervous patients, especially those with high metabolic rates, require a greater induction time and larger concentrations of the gas. An initial potency of 5 to 10 per cent cyclopropane with 90 to 95 per cent oxygen is satisfactory in most cases and the operation can usually be continued with the lower limits of concentration. Recourse to ether as an adjunct to cyclopropane has not been found necessary in our experience. There is no excitement period and the various stages of anesthesia—induction to deep narcosis—are merged rapidly, but the patient is always protected by a large concentration of oxygen. Even passive breathing is compatible with safety. Unlike nitrous oxide, it does not produce choking, burning or strangling. It is pleasant to take. Recovery is rapid. Headache, disorientation and subjective symptoms are reduced to a minimum. Normal conscious reactions are quickly established and the patient can usually cooperate promptly. While postoperative nausea and vomiting occur, we believe that they are less prolonged than with other inhalation anesthetics.

We have been impressed by a peculiar mottled ruddiness of the skin of the body—notably the chest—that very quickly develops after the administration of cyclopropane. The phenomenon seems to be most pronounced in the cases of marked clinical activity and elevation of the B.M.R. It is probably the result of various factors such as the increased concentration of oxygen in the blood and the heightened vasomotor activity. The elimination of the cyclopropane in part by the skin may be an added factor.

In exophthalmic goiter with high metabolism, the patient's demand for oxygen is frequently so great that we have often had difficulty in maintaining a sufficient degree of concentration of nitrous oxide to prevent anoxemia and cardiorespiratory distress. Frequently ether had to be supplemented to obtain relaxation. Venous congestion during the operation was at times disturbing, the postoperative nausea and vomiting were increased, the normal postoperative conscious responses were delayed and acidosis and acetonuria were encountered more often.

Inasmuch as a large number of goitrous patients have varying amounts of

cardiac damage, a powerful anesthetic which per se has no serious toxic effects on cardiac muscle and which can be given without producing anoxemia and consequent overloading of the heart should have distinct advantages. Cyclopropane is such an agent. Most thyrocardiac patients demand more than the ordinary amounts of oxygen. Furthermore, high oxygen ratios protect the weakened myocardium against the strain of operation.[5]

Obstruction to respiration tends to labored breathing and oxygen insufficiency with obvious difficulties. In removing large adenomatous goiters, particularly those that have caused tracheal narrowing or compression, cyclopropane has proven to be very helpful. The tracheal reflexes are quickly abolished and sufficient oxygen can usually be supplied to prevent respiratory distress, venous congestion and asphyxia even with passive breathing. The quick abolition of the throat reflexes by cyclopropane is of great value when recourse to airways seems necessary, particularly in cases of partial obstruction or tracheal narrowing. With other forms of inhalation anesthesia, it is frequently very difficult to insert and maintain the tube on account of troublesome coughing and even vomiting. The resulting dyspnea, cyanosis and venous engorgement produce added difficulties. Anxious moments for anesthetists and operator alike have been less frequent since we have been using cyclopropane.

Because cyclopropane has not been found, experimentally, to depress liver and kidney function excepting when used in exceedingly high concentration, we have found it valuable in long standing cases of hyperthyroidism with hepatic and renal parenchymal damage.

Experimentally, cyclopropane and nitrous oxide were administered interchangeably for varying periods. The change from cyclopropane to nitrous oxide was usually quite noticeable. The respirations quickened and became more active and forceful, the blood became darker and the operative reactions were increased. Whenever nitrous oxide alone or in combination with ether proved to be annoying, a change to cyclopropane was usually promptly followed by calm and relaxation.

It is not within the scope of this brief report to outline our statistical data in great detail. There were only four postoperative developments worthy of mention.

(1) In a woman, age 36, pulmonary embolism and infarction followed almost immediately after operation for Graves' Disease. She continued acutely ill for 12 hours and then steadily improved. Recovery was complete.

(2) A man, age 29, presented an acute Graves' syndrome. Outstanding features were great anxiety and morbid fear of operation. The element of fear was doubtless concerned in a delayed but transiently critical postoperative reaction—a kind of atypical shock that remains unexplained. Recovery followed.

(3) A woman, age 51, suffering from a huge bilateral adenomatous goiter that had recently undergone malignant degeneration was submitted to a partial bilateral lobectomy under cyclopropane. Notwithstanding a prolonged opera-

tion with more than average loss of blood, the condition of the patient as based on the usual criteria, such as pulse, blood pressure and respirations, seemed compatible with safety. A moderately severe shock followed operation. Recovery followed. Study of this case suggests that "surcharging" the circulation, so to speak, with oxygen may at times obscure the real status of a debilitated patient. Such a patient's ruddy appearance may belie her real physical condition and the surgeon may be caught off guard and thus be led into a false sense of security.

(4) There was one fatality. A woman, age 66, who for many years had had a large bilateral adenomatous goiter causing tracheal narrowing, died in crisis 76 hours following operation. (Just how crisis is produced is difficult to say. It is doubtless a summation of a series of reactions involving the thyroid, adrenals and the sympathetic nervous system and precipitated by operative procedures—whether slight or extensive. It may follow after minimal procedures such as a single ligation under local anesthesia.) Critical study of the factors concerned in the fatal crisis leads us to believe that the result was in spite of, rather than because of, the cyclopropane. Incidentally, this was the first fatality in 447 consecutive operations for goiter.[1]

From October 25, 1935, to April 6, 1936, 170 hyperthyroid patients were submitted to operation. Of these by far the greatest number, namely 111 patients, were given cyclopropane-oxygen anesthesia *alone* with generally very satisfactory postoperative results.

The second largest number, namely, 33 patients, were submitted to nitrous oxide-oxygen induction. Nitrous oxide-oxygen was continued, but varying amounts of ether had to be given to maintain satisfactory anesthesia.

The third largest number, namely, 14 cases, were given cyclopropane and nitrous oxide interchangeably in order to study comparative merits. The results were generally in favor of cyclopropane.

A fourth group, namely, eight cases, were given only nitrous oxide-oxygen anesthesia with very satisfactory results. These cases, for the most part, presented the milder degrees of hyperthyroidism.

Three cases were give avertin (basal) anesthesia followed by cyclopropane. One case was given local anesthesia (novocaine) plus cyclopropane.

Three cases were complicated by pregnancy. It is our feeling that pregnancy, particularly in the early months, does not contraindicate operation. On the contrary, we believe thyroidectomy insures a safer labor. In the past, we have held to the opinion that ether in combination with comparatively low concentrations of nitrous oxide was the anesthetic of choice. Nitrous oxide in large concentration was said to predispose to miscarriage especially in the presence of any considerable degree of anoxemia tending to fetal asphyxia. Our three cases made uneventful recoveries and there were no signs of threatened abortion.

In conclusion, we believe that a review of a series of goiter operations performed since October 25, 1935, has indicated that in cyclopropane we have a valuable aid in the facilitation of thyroidectomy. We are of the opinion that

nitrous oxide compares favorably with cyclopropane in the less active and uncomplicated cases of hyperthyroidism. However, in the acute cases with marked clinical activity, high metabolism and cardiac impairment, and in the chronic cases with obstructive difficulties, renal and hepatic parenchymal damage, cyclopropane will doubtless replace nitrous oxide and ether as the anesthetic of choice. Care should be exercised lest hyperventilation obscure the real status of a markedly debilitated or anemic patient. Also it must be borne in mind that hyperoxygenation may lead to unnecessary and annoying apnea. We are hopeful that with further study and experience, the favorable results of thyroidectomy will be further enhanced. Our anesthetists believe—as do we—that cyclopropane represents one more step in the approach to the ultimate, ideal anesthetic.

Note: Prolonged and disturbing apnea occurred once since the preceding report. A careful review of the data relating to the conduct of anesthesia leads us to believe that prolonged hyperoxygenation (with little or no cyclopropane) was the cause. Greater experience should obviate similar occurrences.

In our desire to prevent anoxemia and in view of the ease with which it can be prevented by increasing the oxygen concentration, we should not lose sight of the fact that high percentages of oxygen may of themselves prove toxic and furthermore that hyperventilation per se may lead to apnea.[4] The resultant decrease in the carbon dioxide concentration in the blood may be depressed still further by continued hyperoxygenation and the respiratory center may thus lack the necessary stimulus to respond. A vicious cycle leading to prolonged apnea and even acapnea may thus result—the more the oxygen, the less the carbon dioxide concentration in the blood and consequently the greater and more prolonged the apnea. Even this circumstance, if recognized in time, need not necessarily prove dangerous inasmuch as respiration invariably fails before circulation.[2] When lack of experience or technical error lead to this annoying situation, removal of the mask and artificial respiration should promptly restore spontaneous breathing. Inflation of the lungs with carbon dioxide would occasionally seem indicated to cut short the continued apnea.

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THE PROBLEM OF MYOSITIS OSSIFICANS PROGRESSIVA

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THE study of myositis ossificans progressiva (Münchmeyer's disease), a condition occurring especially in boyhood, still presents many unknown problems. Recent researches of the calcium content of blood (Zieliński[19]) appear to demonstrate a close relationship with parathyroid activity, and the influence of the latter on pathologic bone formation points decidedly to an endocrine imbalance that gives rise to various morphologic conditions which are, no doubt, the result of a trophic degeneration.

From the histogenetic point of view it is a progressive bone metaplasia of different muscular groups, of the fasciae and of the tendons. Generally speaking, myositis ossificans progressiva commences by attacking the muscles of the neck, shoulders, and thoracic wall, as well as those of the trunk and mastication (Frejka,[5] Guilbert,[7] Westman,[18] Hickel,[8] Rinderman,[12] Fischer,[4] Rouis,[15] Magruder,[9] Apert and Garnier,[1] Rocher,[13, 14] Cassar and Jaubert de Beaujeu,[2] Masselot, Jaubert de Beaujeu and Bloch,[10] Sàlat,[16] Dobrzaniecki[3]). The localization in the lower parts of the body, such as in the rectus abdominalis, is most unusual. I have not found any instance of its having occurred in the muscles of the lower extremities. The smooth muscles of the vegetative organs and the striated muscles of the face, eyes, diaphragm, heart and of the sphincters, always remain intact.

In addition to the bone metaplasia one may also find abnormal cartilaginous exostoses which may form elastic tumors under the skin, and even serous bursae, representing true hygromata.

The disease may manifest itself very early in infancy, but rarely occurs in individuals over 20 (Apert and Garnier[1]).

The prognosis is quite unfavorable on account of the limitation of movements, particularly those of mastication and respiration, which finally results in progressive cachexia.

There does not appear to be at present any appropriate treatment, either conservative or operative, although many attempts have been made such as the use of roentgen therapy (Nové-Josserand and Horand, Mucklow,[11] Schinz-Baensch-Friedel[17]), diathermy, treatment by mesothorium and hot air, internal acidifying treatment (Froehlich), fibrolysin, potassium iodide and recently parathryroidectomy (Rocher and Mathey-Cornat[14]), endocrinotherapy (Gorlitzer[6]) and removal of calcium from the food.

Based upon the literature we do not believe this disease to be hereditary, as some authors maintain; but it is certain that it has some predilection to males.

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In certain cases one finds, in the anamnesis, the occurrence of syphilis in the parents, in other cases a concomitant tuberculosis.

Case Report.—A boy of four and one-half years was admitted to the hospital because of the abnormal position of his head, which had previously been diagnosed as torticollis. The parents could not state exactly when the condition had begun. The inclination of the head, however, had appeared eight months before. The physical and psychic state of the child was distinctly impaired.

The skin and the mucous membranes were pale. The abnormal position of the head

FIG. 1.—Inclination of the head towards the sternum with slight rotation to the right resulting from the ossification of the muscles of the nape of the neck. (Claude Bernard, Horner's syndrome of the left eye.)

FIG. 2.—On the nape of the neck is seen a protuberance extending archwise from the occiput on the right to form one mass with that on the thoracic. On the opposite side the protuberance commences at the level of the third rib and is less marked. These major masses are covered along their course by multiple exostoses.

was striking (Fig. 1), but it differed considerably from that of an habitual torticollis. It remained inclined downwards, with the chin fixed to the sternum, and it was impossible to obtain any movements of the head, either actively or passively, as the skull and the vertebral column were apparently rigidly fused. There was also an intense constriction of the jaw, which we were inclined to attribute to a process of a commencing myositis, as the roentgenologic examination of the temporomandibular articulation and of the muscles of mastication showed nothing that could explain the trismus in any other way. The configuration of the face was symmetrical. The left eye showed a very distinct Claude Bernard-Horner syndrome.

Deep palpation of the neck did not disclose any tumefaction of the parathyroids.

On the nape of the neck a protuberance could be seen that extended from the occiput on the right side to the thoracic tumefaction on the same side. On the opposite side the tumor which commenced at the level of the third rib was less distinct. These major masses gave rise to a lateral tumor (Fig. 2). They were all easily palpable, of a bony consistence, and contained many excrescences of different dimensions which gave one the impression of cartilage. These exostoses were firmly attached to the deeper structures. One of them was removed (Fig. 3) together with a newly formed bony fragment for microscopic examination, which showed a normal cartilaginous bony structure with a medullary canal.

FIG. 3.—The cartilaginous exostosis removed with a fragment of a newly formed bone for microscopic examination.

There were other developmental anomalies present. The thumb was brachydactylic inasmuch as it showed a reduction in its length. The feet were flat, and the toes were in the position of the hallus valgus.

Roentgenologic Examination.—The skull and sella turcica were normal. The feet showed moderate widening and elongation of the shafts of both first metatarsal bones, with quite pronounced thinning of the cortex and increased lamellation in the medullary area. The course of these trabeculae deviates from that of the normal trabeculation; some

FIG. 4.—Roentgenogram of the feet, showing the toes in hallus valgus position, and the increased lamellation in the medullary area of the first metatarsal. The lack of distinct differentiation between the compact and the cancellous tissue may also be noted.

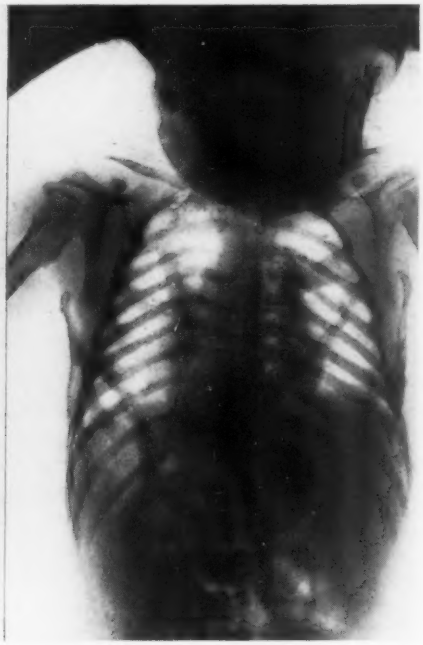

FIG. 5.—Anteroposterior roentgenogram of the neck and thorax.

FIG. 6.—Lateral roentgenogram showing the ramifications in the thoracic muscles and along the vertebral column.

FIG. 7.—Roentgenogram showing a detail of the synosteosis of the cervical ossification with the occiput.

FIG. 8.—Roentgenogram showing a detail of the lumbosacral ossification.

appear thicker than normally. The remaining metatarsals, with the exception of the second and third left, and also all the tarsal bones, present similar structural changes to a lesser degree (Fig. 4). There is no distinct differentiation between the compact and the cancellous tissue. The distal ends of both first metatarsals present a deformity resembling an epiphysis, which, however, is not normally present.

A tuberculous subclavicular focus was evident in the apex of the left upper lobe of the lung.

The anteroposterior roentgenogram of the neck and thorax was most instructive as far as the anatomic disposition of the ossifications was concerned (Fig. 5). Generally speaking, these formed two large masses along the vertebral column, beginning on the left side from the third thoracic vertebra and on the right from the occiput where they formed the true synosteosis. The ossified streaks extended as far as the iliac crests. Thus the process affected all the muscles of the nape of the neck and an entire mass of the dorsolumbosacral group. These ossifications continued, through their ramifications, to the thoracic muscles. In three places the new ossified formations presented buds of articulations, either among themselves or with the vertebrae (Figs. 6, 7 and 8). A composite tracing made from the roentgenograms gave us an exact insight into the dimensions and the courses of the ossified muscles (Fig. 9).

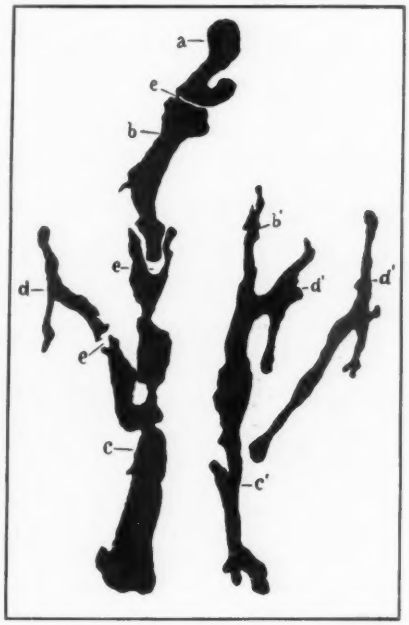

FIG. 9.—A composite tracing of the roentgenograms showing the dimensions and the course of the ossified muscles. (a) Cervical ossification, (bb') Ossifications along the vertebral column, (dd') Ramifications in the thoracic muscles, (cc') Lumbosacral ossifications, (e) Buds of articulations.

In addition to these disturbances there were also found on the internal border of the proximal diaphysis of the humerus and of the left tibia, formations similar to osteogenic exostoses.

The Bordet-Wassermann reaction was negative. The calcemia indicated by the Kramer-Tissdal method was 19.5 milligrams per cent (normal 7.9 milligrams per cent). The urinalysis was normal.

We contemplated, primarily, making an exploratory incision in the neck in order to examine the parathyroids. This, however, was impossible, owing to the position of the head, as the jaw completely covered the anterior surface of the neck. We therefore restricted ourselves to roentgen therapy of the parathyroids. On examination of the calcium content of blood three months later, the recovery of 19.67 milligrams per cent showed that the calcemia had been maintained at its original level.

During the course of the child's illness there persisted a continued elevation of the temperature, which reached a maximum of 39° C. This lasted for two weeks without any positive clinical sign that would explain it. We were inclined to attribute it to the tuberculous subclavicular focus which had been disclosed by the roentgenologic examination.

The child remained under our observation for three months, during which time the disease made further progress in the muscles of the thoracic wall and of the lumbar region.

We must admit here that the term "myositis ossificans progressiva" is not very rightly chosen, if we consider this affection as a constitutional anomaly,

or as an osteoformatory aberration, a hormonal disturbance or a vicious differentiation of the mesenchymatous elements. The term myositis is therefore inexact and requires a revision in order to more correctly adapt it to the present ideas concerning this disease.

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DIVISION OF RIBS AS AN AID IN CLOSING A DIAPHRAGMATIC HERNIA

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IN HEDBLOM'S reviews[1, 2] reference is made to thoracoplasty as a preliminary to the repair of large defects or congenital absence of the diaphragm on the left. Carrington[3] and Harrington[4] appear to have been the first to carry out this two stage technic. No doubt, also, the simple section or resection of small segments of the lower ribs at the time of operation has been made use of to accomplish a less complete collapse of the thoracic cage, but, although the rationale seems obvious and the procedure itself surprisingly simple, I am unable to find the record of more than two cases in which the maneuver has been utilized. These were reported by Bettman and Hess,[5,6] who in 1929 and 1931 successfully operated upon infants of three and one-half, and nine months, respectively, by their original technic.

In my own case, the repair was made so much more simple and secure by removing small segments of the ninth, tenth and eleventh ribs that I am sure similar cases can be benefited by use of the method. This feeling is substantiated by descriptions in the literature of cases in which recurrences of peripheral defects in the diaphragm were ascribed to inability to close satisfactorily the portions which lay next to the ribs. In some of these cases the section and inward displacement of the ribs would undoubtedly have led to success.

In the case cited, the ribs dropped inward, thus releasing tension so that the mattress sutures of braided silk which had been placed in the diaphragm could be tied without undue strain, and so that the outer arms of the defect could be sutured securely to the displaced ribs, completing the closure (Fig. 6a, b, c).

Case Report.—J. S., a boy, age eight, had been observed by members of the pediatric service since the age of three. His birth and early development were normal, but when he was two and one-half years old he fell about eight feet to the ground from the top of a shed, striking forcibly on the left side of the body and fracturing the left forearm. The child was quite ill and somewhat short of breath for a few days after this accident, but attention was paid for the most part to the broken arm. There were no gastro-intestinal symptoms until six months later when the child was admitted to the pediatric ward because of vomiting, indigestion and diarrhea. Investigation revealed a dextrocardia and an abnormality of the left chest which was at first interpreted as chronic empyema (Fig. 1). However, peristaltic sounds were heard and roentgenologic examination demonstrated the presence of loops of bowel in the left pleural cavity (Fig. 2). When filled with barium, the stomach was seen to be large and atonic (Fig. 3), and a

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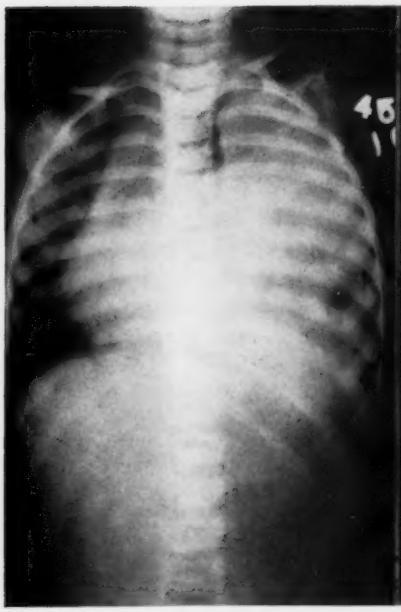

FIG. 1.—Original roentgenogram at the age of three.

FIG. 2.—Roentgenogram taken a few days after that shown in Fig. 1, in which the loops of bowel are more evident.

FIG. 3.—Dilated, atonic stomach. (This dilatation of the stomach was important because it kept the peritoneal cavity large enough to receive the intrathoracic viscera at operation.) No evidence of small intestines in the peritoneal cavity. Gas in colon indicates site of hernia in diaphragm.

FIG. 4.—Barium enema showing colon high in the left thoracic cavity. In a lateral film, narrowing of the lumen was seen at the orifice of the diaphragmatic defect.

barium enema showed that a large part of the otherwise normal appearing colon was above the diaphragm (Fig. 4).

The child's indigestion and diarrhea ceased and he was discharged much improved. From this time on, however, he was in and out of the hospital and dispensary repeatedly, once with measles, but usually with mild or severe upper respiratory infections or mild colic and vomiting accompanied by diarrhea. The symptoms always subsided quite promptly when he was put to bed, but he remained somewhat thin, frail and undersized. The mother was advised in 1932 that an operation should be performed, but it was not until after a rather severe attack of obstruction in 1935 that she consented.

Fortunately, this acute attack subsided. Further roentgenologic examination then showed that during the five years since the original studies the left lung had expanded somewhat, and the heart had approached the midline (Fig. 5). The stomach still hung low in the pelvis, but was less atonic. No loops of small bowel were ever visualized in the abdomen. A barium enema showed the colon situated as formerly with all of it, except the sigmoid and descending arm, in the left thoracic cavity.

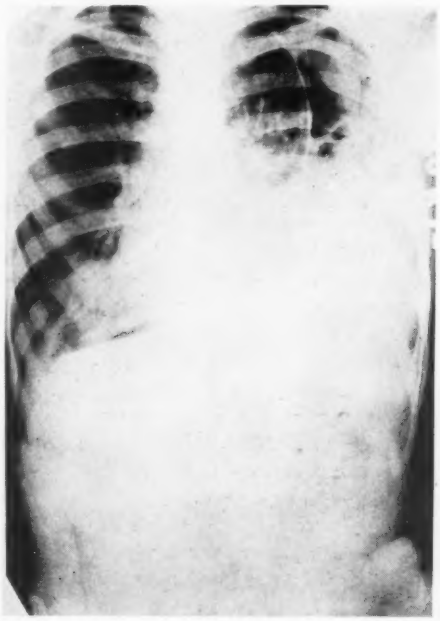

FIG. 5.—Roentgenogram made at the age of five, before operation. The lung has expanded somewhat and the heart is nearer the midline. (Compare with Fig. 1.)

Operation: Preliminary Abdominal Exploration.—In order to determine the exact relations of the viscera within the abdominal cavity, an upper left rectus incision was made under ether anesthesia July 10, 1935. The stomach was atonic and filled a large portion of the abdominal cavity. The edge of the liver lay just above the level of the umbilicus. A Levine tube was passed and through it the stomach was emptied of gas so that it was possible to displace it and thus visualize the other abdominal viscera. The rectum, sigmoid and descending colon extended straight from the pelvis to the lateral portion of the left leaf of the diaphragm where the colon entered the thoracic cavity. The spleen was nowhere to be seen and a large part of the omentum was in the thorax. On observing the stomach more carefully, it was seen that the fundus was just below the hernial orifice, while the body hung low into the false pelvis, and the pylorus was hooked up high under the liver. The duodenum extended straight upward to the medial edge of the defect in the diaphgram; only about 8 cm. of the duodenum were within the abdominal cavity, and no other small bowel was to be seen. The gallbladder was normal except for a slight, apparently recent, low grade plastic peritoneal reaction which involved the visceral and parietal peritoneal surfaces here and elsewhere throughout the upper abdomen. The kidneys were normal in size and position, but the pancreas was pulled upward toward the hernial orifice, which was placed laterally and measured approximately 8 by 6 cm. The end of the ellipse which lay against the wall of the chest was somewhat broader and more firmly fixed than the narrower internal end which was not far from the esophageal orifice. The adhesions of omentum and bowel to the under surface of the diaphragm were not extensive. There was no adverse reaction to this exploration.

Secondary Thoracic Procedure.—Three days later, again under ether anesthesia, the thorax was opened through the eighth intercostal space. The spleen was encountered

immediately and was found covered with the same thin, plastic exudate which we had noted in the abdomen. The ribs were spread widely, and the hernial orifice in the diaphragm was palpated. It lay against the wall of the chest in the anterior axillary line and extended toward the esophagus. Through it passed bowels and omentum. There was no peritoneal sac. The entire small bowel and the proximal half of the large bowel and the spleen were intrathoracic. The lung could be seen at the apex of the pleural cavity, small and covered by thickened pleura. The viscera were somewhat suspended in the thoracic cavity by numerous adhesions which were carefully separated by sharp and blunt dissection. A few were divided between ligatures.

The defect of the diaphragm was outlined by sharp dissection and the hand was passed into the abdominal cavity to make sure that reduction of the viscera would be made directly into the free peritoneal cavity. The spleen was first reduced, followed by the large and then the small bowel. It was necessary to increase the size of the opening by a medial incision in order to accomplish reduction. Even then the last portion of the small bowel was replaced with difficulty and had to be held in place by Mikulicz pads while the repair was carried out. The left phrenic nerve was not seen and the diaphragm did not move with respiration. Nevertheless, the musculature of the diaphragm was not atrophic and was well nourished.

The opening which had to be closed measured about 8 cm. in length and 6 cm. in width. At the medial end of the defect there was no difficulty in placing and tying mattress sutures of heavy braided silk, producing an overlap of at least 1 cm., but on progressing toward the ribs the diaphragm became more and more fibrous and fixation of the scar to the ribs made an unbridgeable gap of almost 5 cm. By retracting and freeing the soft tissues, the ninth, tenth and eleventh ribs were exposed slightly posteriorly to the defect in the diaphragm and segments about 1 cm. long were excised subperiosteally from each of them. It was now easy to foreshorten the wound in the diaphragm by passing braided silk sutures around these freed ribs and by suturing the diaphragm firmly to them up to a point where the original overlap could be made secure. The repair was thus made in a T-shaped manner and the central sutures passed through the outer end of the 1 cm. overlap (Fig. 6a, b, c). Interrupted figure-of-eight sutures of fine silk were placed to tack down the free edge of the diaphragm. The cavity in the chest seemed quite large and the lung, which measured only about 5 by 8 cm., showed no tendency to expand. The pleura over it was thick and white and there were several firm adhesions connecting its upper portion to the cupola of the pleura. It seemed best not to disturb these adhesions because the dissection would have to be done at the ends of long instruments and should any difficulty in hemostasis be encountered the bleeding would be difficult to control. Then, too, the child could not stand safely any further operating. The chest wall was closed hermetically by circular approximation of the two ribs adjoining the wound followed by careful suturing of the fascial layers with silk.

Stained smears and cultures of the plastic exudate found over the spleen showed no organisms.

The convalescence following this rather extensive replacement of viscera and closure of the diaphragm was surprisingly smooth. A transfusion of 250 cc. of blood was given immediately postoperative and fluids were provided in adequate amounts by mouth, subcutaneously and intravenously during the following days. There was no occasion to aspirate air from the left pleural cavity; however, as has been pointed out by many writers, this should be done in most cases immediately after the chest is closed. An oxygen tent was unnecessary. The intranasal Levine tube used at operation was left in place with constant negative pressure applied to keep the stomach and upper bowel free from gas. Castor oil and eserine were given to promote peristalsis, and the patient expelled gas through a rectal tube the day after operation.

The roentgenogram shown in Fig. 7 was taken on the sixth postoperative day when the temperature was 98.4° F., pulse 80, and respirations 20. There was no distress in spite of the shift of the heart to the right, apparently because the child had adjusted him-

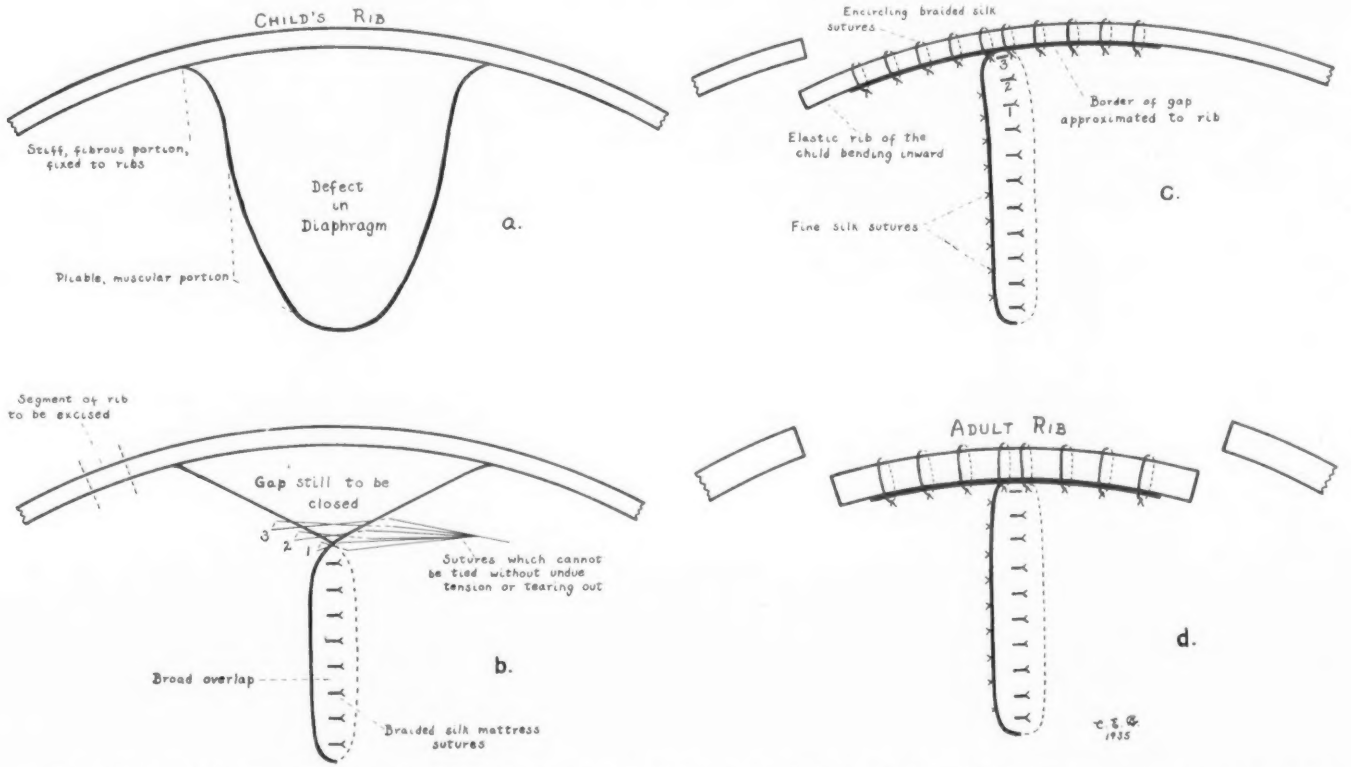

FIG. 6 (a, b and c).—Shows the successive steps in the closure of the defect in the diaphragm in the author's case; (d) suggested technic for adults whose ribs are less yielding. In children one segment is removed from each rib; in adults two segments are excised. It will be recognized that the figures are diagrammatic and that, due to the obliquity of the ribs in relation to the periphery of the diaphragm, it is necessary to remove segments from at least two ribs in order to obtain the desired relaxation. Furthermore, of course, the diaphragm is sutured to two or three of the mobilized ribs instead of one.

FIG. 7.—Roentgenogram made on the sixth postoperative day. There was no respiratory distress and the temperature and pulse rate were normal. The figure shows the overlapping ribs (9, 10, 11) from which segments were removed and to which the diaphragm was sutured.

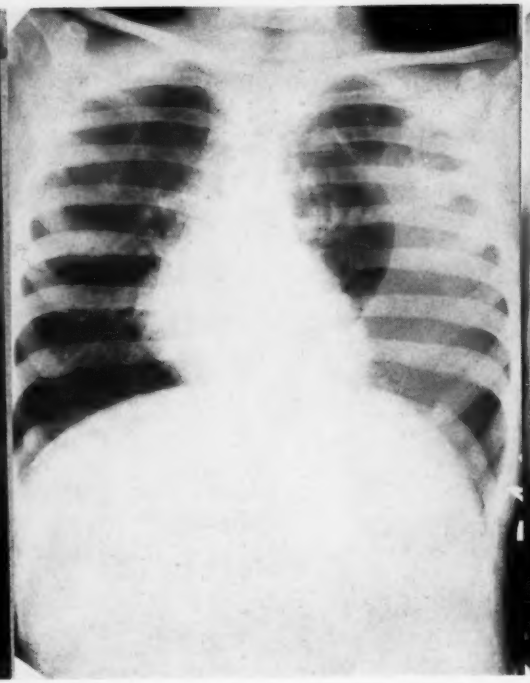

FIG. 8.—Three weeks after operation. The lung is expanding slowly and the heart is returning to the left side of the thorax.

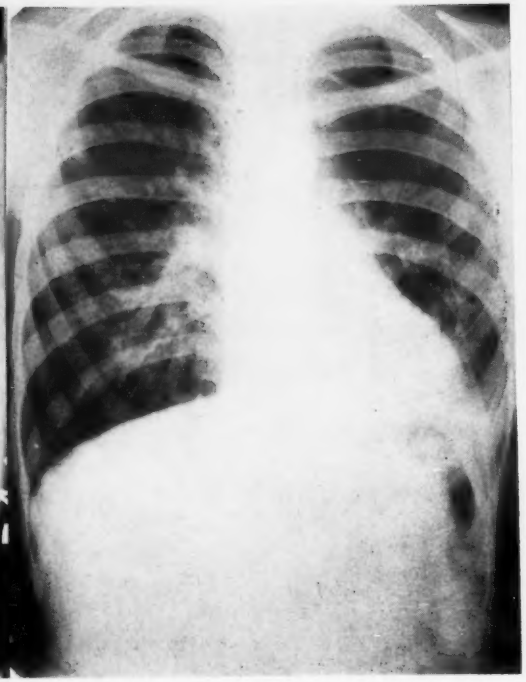

FIG. 9.—Four months after operation. Further expansion of the lung. Heart pulled over to the left.

self to a reduced vital capacity over a period of years. The roentgenogram shows well the three displaced ribs from which short segments were taken in order to allow satisfactory closure of the diaphragm without undue tension. The thoracic wound healed cleanly.

Subsequent studies with barium by rectum and by mouth showed the colon, stomach and small bowel to lie in slightly bizarre relationships, but their functions were normal. A month after operation the child ate five green apples and a peach and gave everyone

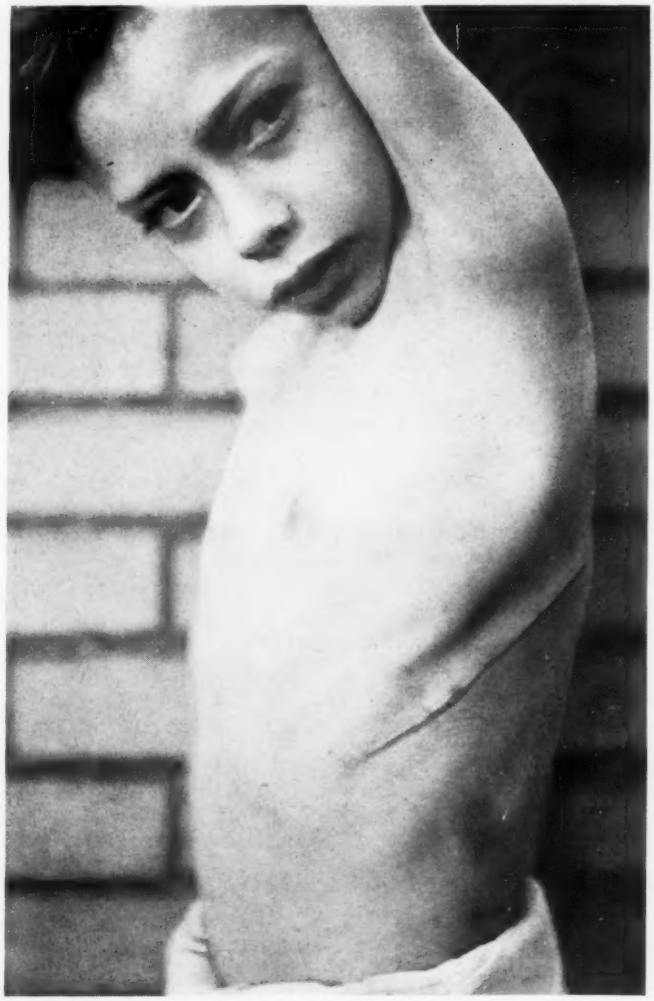

FIG. 10.—The photograph shows the thoracic incision through which the repair was carried out.

a scare because of colic and vomiting, but otherwise there has been nothing to suggest intestinal obstruction or recurrence of the hernia.

A roentgenogram of the chest taken three weeks after operation showed beginning expansion of the left lung, also density indicative of fluid in the pleural cavity (Fig. 8). Postero-anterior (Fig. 9) and lateral films taken four months later indicate that the lung is expanding slowly in spite of the thickened and adherent visceral pleura, and the probability is that expansion will be complete within a short time. The vital capacity is 1,000

cc. when lying down, and 1,200 cc. when standing up. The child's mother says that whereas formerly he never ran and played because of shortness of breath, he now runs upstairs without dyspnea and plays normally. She has noted also that previously the thorax appeared full and the abdomen usually flat. Now the left chest is slightly depressed and the abdomen is rounded (Fig. 10). The child's weight has increased from 40 to 47½ pounds during the six months since operation.

CONCLUSIONS

The simple maneuver of mobilizing two or three of the lower ribs is useful whenever the diameter of the lower thoracic outlet must be diminished in order to close a defect of the diaphragm satisfactorily. This is easily accomplished in children. In older patients, whose ribs are unyielding, the removal of two short segments from each rib, one segment anterior to the defect and the other posterior, will allow the ribs to drop in sufficiently, without damage to intercostal vessels, nerves or the pleura, to effect a repair in some of the difficult cases (Fig. 6d).

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DIVERTICULA OF THE VERMIFORM APPENDIX

A STUDY BASED ON THIRTY CASES

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IT IS becoming increasingly more apparent that diverticula of the vermiform appendix should merit more than mere academic interest on the part of physicians. Acute inflammation occurring in an appendix containing such diverticula is commonly followed by rapid perforation through the diverticulum with a subsequent generalized peritonitis after only a very few hours of atypical abdominal signs and symptoms. Mucoceles developing in appendices that possess diverticula quite commonly perforate and cause pseudomyxoma peritonei. The data embodied in this study have been collected during the past ten years.

Appendiceal diverticula may be classified into two groups; the congenital or true and the acquired or false. Congenital diverticula are rare. The walls of such a diverticulum contains all the normal histologic components of the appendiceal wall. This group either develops during the growth of the fetus or before inflammatory changes make their appearance in the appendix. Edel, in 1894, reported one of the first examples of this type. The second type, or acquired false diverticulum, is commonly referred to as the inflammatory type, because it originates secondary to a preceding appendicitis which has left in its wake stenosing scars that cause varying degrees of lumen occlusion. The efforts of the muscularis of such an appendix to empty its lumen commonly lead to marked increase of the intraluminal pressure which in turn causes, occasionally, the herniation of the mucosa out through areas of lessened resistance in the muscularis which are the vascular hiati. Thus, the walls of the acquired or false appendiceal diverticulum are only composed of mucosa, some loose areolar tissue and the serosa. Therefore, the mechanism for sudden perforation during the acute inflammation of such an appendix is apparent.

The following is a brief review of some of the important contributions made upon this subject in the past: Villar[35] (1819) described an instance of perforation of an appendiceal diverticulum with the subsequent formation of a generalized pseudomyxoma peritonei. Excellent pathologic descriptions were presented by Rokitansky[29] (1842), Gähtgen[9] (1853), and Virchow[36] (1863). Heschl[15] (1880) experimentally reproduced false diverticula of the intestine by removing portions of dead human intestine and distending them with water under increased pressure. He found that small areas of bulging could be observed to occur along the mesenteric border which again

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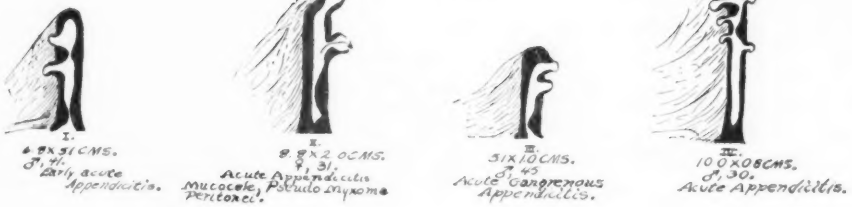
disappeared when the water pressure was reduced. Heschl believed, therefore, that obstruction plus increase of internal pressure in a hollow viscus were the two chief factors responsible for false acquired diverticulum formation. Hansemann[13] and also Grassberger[11] (1897) independently confirmed Heschl's observations. Weinberg[39] (1898) presented his thesis upon the histologic lesions and common types of appendicitis. In this study, he discussed diverticula formation. He considered that they arose following repair of the mucosa after deep ulceration of the muscularis had occurred. It was his belief that either perforation occurred; or if the process stopped short of actual perforation, a diverticulum of the wall might be the result. Chlumsky[6] (1899) proved that Heschl's (1880) experiments were invalid, because he had used dead intestine. When Chlumsky repeated this work using living dog intestine, acquired diverticula formation did not occur along the mesenteric border. When the excessive internal pressure finally burst the loop of intestine, it always occurred along the antimesenteric surface. Beer[4] (1904) substantiated Chlumsky's claims.

Mertens[23] (1902) maintained that diverticula formation in the appendix occurred in the region of the vascular passages through the appendiceal muscularis. He believed in the presence of acute appendicitis, that rapid perforation with few symptoms could happen in such a diverticulum. The straining attendant upon defecation was also thought to occasionally rupture an appendiceal diverticulum. Mundt[26] (1903) concluded that diverticula of the appendix resulted from a circumscribed local infection of the appendiceal wall with destruction of the muscularis. After healing this gave rise to an extrusion of the mucosa through the appendiceal wall. It was his opinion that inflammation was the chief etiologic factor in the causation of appendiceal diverticula. Hedinger[14] (1904) reported an instance of a congenital diverticulum of the appendix which was present in a full-term stillbirth consequent to a protracted labor as the result of a hydramnion and a transverse presentation. The distal third of the appendix was studded with numerous varying sized diverticula. Microscopic examination showed that these were of the congenital type and that the crypts of Lieberkühn showed increased branching with an accompanying tall and cylindrical mucosal epithelium. Von Brunn[37] (1905) and Seeling[31] (1906) added six examples of acquired diverticula to the literature. Seeling's case was noteworthy because the diverticulum extended through a vascular hiatus in the muscularis. Maale[19] (1908), in a small carefully studied group of appendices, was able to find eight additional examples of the inflammatory type. MacCarty and McGrath[22] (1911) from their study found that appendiceal diverticula were usually multiple. Fifty-six per cent of their cases were derived from instances of acute appendicitis. The average age at operation in this series was 34 years with the extremes varying from 18 to 64 years. The average duration of symptoms had been seven years. Krabbel[17] (1912) stated that

PLATE 1.



I. 6.8 x 3.1 CMS. ♂ 14. Early acute Appendicitis.

II. 8.8 x 2.0 CMS. ♀ 31. Acute Appendicitis Mucocele, Pseudo Myxoma peritonei.

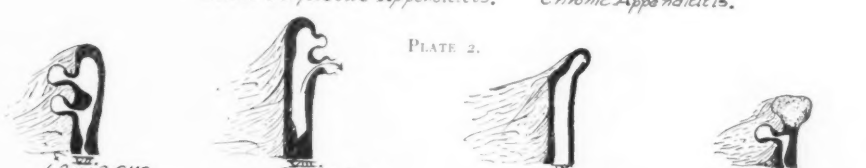
III. 5.1 x 1.0 CMS. ♂ 45 Acute Gangrenous Appendicitis.

IV. 10.0 x 0.8 CMS. ♂ 30. Acute Appendicitis.

V. 7.0 x 1.0 CMS. ♀ 27. Acute Perforative Appendicitis.

VI. 7.8 x 0.8 CMS. ♀ 14. Chronic Appendicitis.

PLATE 2.



VII. 6.2 x 1.3 CMS. ♂ 30. Acute Appendicitis.

VIII. 8.0 x 1.5 CMS. ♂ 49. Pseudo-Myxoma-Peritonei-Mucocele.

IX. 6.4 x 1.4 CMS. ♀ 33. Chronic Appendicitis.

X. 4.0 x 0.7 CMS. ♂ 51. Subacute Appendicitis; Carcinoid Tumor of Ap.

XI. 11.4 x 1.6 CMS. ♂ 64. Chronic Appendicitis.

XII. 7.2 x 0.9 CMS. ♂ 32. Subacute Appendicitis.

PLATE 3.

XIII. 8.8 x 1.1 CMS. ♀ 37. Acute Perforative Appendicitis.

XIV. 9.7 x 1.3 CMS. ♀ 43. Early Acute Appendicitis.

XV. 6.1 x 1.2 CMS. ♂ 41. Acute Gangrenous Appendicitis.

XVI. 6.1 x 1.1 CMS. ♀ 43. Acute Appendicitis.

XVII. 7.9 x 0.9 CMS. ♂ 39. Chronic Appendicitis.

XVIII. 8.1 x 1.1 CMS. ♀ 28. Mucocele, Pseudo Myxoma Peritonei, Perforation.

he had never encountered an instance of true congenital diverticulum formation in the appendix.

Aschoff[2] (1913) believed that diverticula resulted from an acute appendicitis causing scar tissue healing and that subsequent distension of the appendiceal lumen leads to mucosal herniations. Sturm[34] (1915) reported two further examples of congenital appendiceal diverticula occurring in stillbirths weighing 1,700 and 1,530 Gm. Grynfeltt and Chauvin[12] (1920) reported an isolated case of inflammatory diverticula. Wilkie[40] (1921) described two cases of carcinoma of the appendix with accompanying diverticula extending into the meso-appendix. In one instance the carcinoma obstructed the lumen at the base of the appendix. Five congenital diverticula were

PLATE 4.

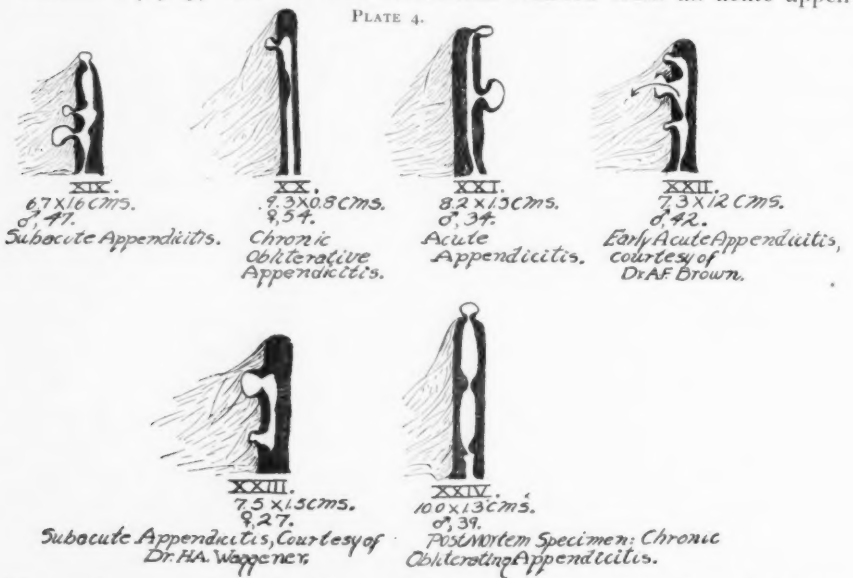
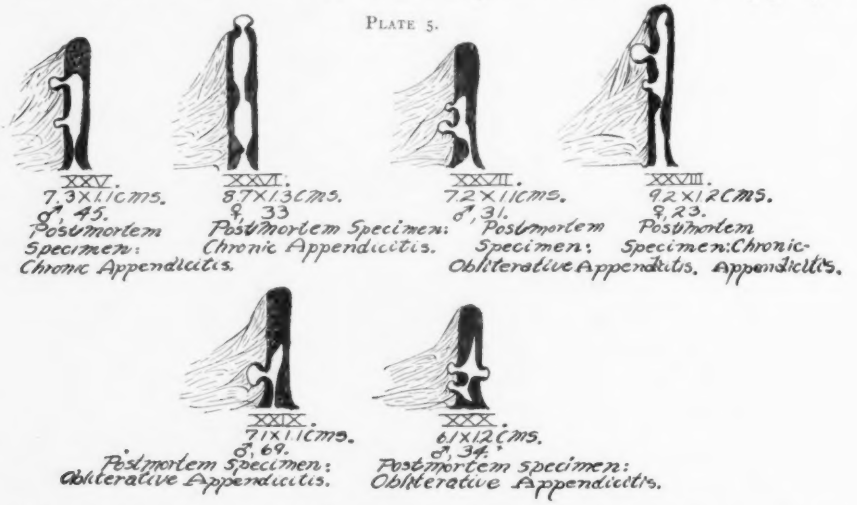


PLATE 5.



present which he believed were formed by the lumen occlusion allowing a secondary increase in the intraluminal pressure to occur. Löhr[18] (1922) subscribed to the inflammatory origin of most appendiceal diverticula. Stout[33] (1923) experimentally injected saline into the submucosa and caused violent contractions of the muscularis to occur with a secondary protrusion of the mucosa and submucosa through the vascular hiatus in the muscularis. Bachlechner[3] (1924) reported an example of a large twisted congenital appendiceal diverticulum occurring at the base in a male, age 17 years. This presented evidence of acute appendicitis. Malone[20] (1924) added an additional example of the congenital type, in which symptoms referable to the appendix had been present for the past six years. Ries[28] (1924) stated that appendices from which pseudomyxoma peritonei may originate are more or less cystic, often show diverticula formation and may contain papillomatous tumors. Such cases in females require careful investigation of the appendix. Chase[5] (1927) believes with Aschoff[2] (1913) that the rapid loss of weight in a patient, allowing loss of adipose and fibrous tissues about a vascular hiatus in the muscularis, could cause a definite weakness in that region which may later be the site of diverticulum formation.

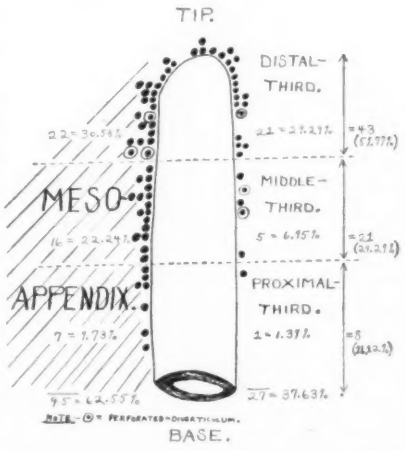


PLATE 6.—Diagrammatic representation of location of each individual diverticulum in this series.

Pack and Scharnagel[27] (1928) believed that appendiceal diverticula exposed the individual to an increased liability to subsequent acute appendicitis, increasing the possibilities of perforation, and that they were often overlooked because they were situated in between the leaves of the meso-appendix. Most instances were of the false inflammatory type. Their material showed an incidence of 0.74 per cent of appendiceal diverticula formation. Masson and Hamrick[21] (1930) described two cases of pseudomyxoma peritonei which originated from perforated appendiceal diverticula. Edwards[8] (1934) found in his material that the average age of the patients was 42 years. All his instances had multiple diverticula and their most favored site of occurrence was along the meso-appendiceal border corresponding to the site of entrance of vessels. In contradistinction to diverticula formation elsewhere in the gastro-intestinal tract which exclusively elect the vascular hiatus through the muscularis, those of the appendix may occur in any situation around the appendiceal circumference.

Table I briefly summarizes the incidence of this pathologic entity as reported in the literature. Table II presents data derived from 60 of the cases included in Table I. The material which forms the basis of this study was derived from 30 cases which I have observed during the past ten years.

Twenty-three of these occurred in 3,017 consecutive appendectomies (0.77 per cent), and the remaining seven examples were derived from 1,054 consecutive unselected postmortem appendices (0.66 per cent). Table III tabulates the important findings in this study, so that a comparison can be easily made with cases previously reported. Plates 1 to 6 graphically describe the individual cases that comprise this study. They are self-explanatory and do not need, therefore, to be reported in detail.

TABLE I

RÉSUMÉ OF INCIDENCE OF APPENDICEAL DIVERTICULA AS REPORTED IN THE LITERATURE

Author	Year	Source of Material	No. of Cases Studied	No. of Diverticula Found	Incidence Per Cent
Mertens	1902	Surgical	106	3	2.80
Beer	1904	Postmortem	106	2	1.99
Beer	1904	Surgical	28	1	3.56
Konjetzny	1909	Postmortem	1,000	2	0.20
MacCarty and McGrath	1911	Surgical	5,000	17	0.34
Moschowitz	1916	Surgical	1,500	4	0.27
Stout	1923	Surgical	264	5	1.89
Chase	1927	Surgical	394	3	0.76
Sauer	1930	Surgical	5,283	9	0.17
Mulsow	1932	Surgical	870	13	1.49
Edwards	1934	Surgical	1,493	8	0.53
		Totals	16,044	67	Av. Incid. 0.42

TABLE II

DATA CONCERNING 60 APPENDICEAL DIVERTICULA REPORTED IN THE LITERATURE *

Sex:	Females	48.3%
	Males	51.7%
Age:	Average age in 54 cases	35.7 yrs.
	Average age for females	40.3 yrs.
	Average age for males	31.1 yrs.

SITE OF LOCATION OF DIVERTICULUM

Tip	28.3%
Middle	55.0%
Tip and Middle	11.7%
Base	5.0%

NUMBER OF DIVERTICULA IN EACH SPECIMEN

One	59.9%
Two	18.3%
Three	5.0%
Four	8.4%
Five	5.0%
Six	1.7%
Seven	1.7%

TABLE II. *Continued*

LOCATION OF BORDER WHERE DIVERTICULUM AROSE

On meso-appendix border	63.3%
Partially from meso-appendix border	10.0%
On antimeso-appendix border	26.7%

PATHOLOGY ACCOMPANYING DIVERTICULA FORMATION

Acute appendicitis	59.9%
Chronic appendicitis	33.4%
Perforation of the appendix	28.3%
Mucoceles and pseudomyxoma peritonei	19.9%
"Carcinoma" of the appendix	8.4%
Congenital type of appendiceal diverticula	13.3%

* Above data derived from reports by: Seeling (1906), MacCarty and McGrath (1911), Wilkie (1921), Stout (1923), Ries (1924), Bachlechner (1924), Malone (1925), von Faykiss (1925), Chase (1927), Gardham, Choyce and Randall (1928), Arnold (1928), Sauer (1930), Stewart (1930), Masson and Hamrick (1930), and Mulsow (1932).

TABLE III

DATA CONCERNING 30 APPENDICEAL DIVERTICULA REPORTED IN THIS SERIES

Sex:	Females	12	39.96%
	Males	18	59.94%

SITE OF LOCATION OF DIVERTICULUM

Tip and distal third	59.77%
Middle third	29.29%
Proximal third	11.12%

NUMBER OF DIVERTICULA IN EACH SPECIMEN

One	9	29.97%
Two	13	43.29%
Three	3	9.99%
Four	1	3.33%
Five	1	3.33%
Six	2	6.66%
Seven	1	3.33%

LOCATION OF BORDER WHERE DIVERTICULUM AROSE

On meso-appendix border	13	43.29%
Partially from meso-appendix border	7	23.31%
On antimeso-appendix border	10	33.30%

PATHOLOGY ACCOMPANYING DIVERTICULA FORMATION

Chronic appendicitis	6	19.98%
Chronic obliterative appendicitis	6	19.98%
Subacute appendicitis	3	9.99%
Subacute appendicitis, carcinoid tumor at tip	1	3.33%
Pseudomyxoma peritonei, mucocele, perforation	3	9.99%
Early acute appendicitis	3	9.99%
Acute appendicitis	4	13.32%
Acute gangrenous appendicitis	2	6.66%
Acute perforative appendicitis	2	6.66%
Congenital true diverticula	2	6.66%

TABLE III. *Continued*

DIMENSIONS				AGE	SEX	
Length in Cm.		Diameter in Mm.		Years	Males	Females
4.0– 4.4	1	0.5	0	0– 4	0	0
4.5– 4.9	0	0.6	0	5– 9	0	0
5.0– 5.4	1	0.7	1	10–14	0	1
5.5– 5.9	0	0.8	3	15–19	0	0
6.0– 6.4	5	0.9	2	20–24	0	1
6.5– 6.9	2	1.0	3	25–29	0	4
7.0– 7.4	6	1.1	6	30–34	6	3
7.5– 7.9	3	1.2	4	35–39	2	1
8.0– 8.4	3	1.3	4	40–44	5	1
8.5– 8.9	3	1.4	1	45–49	2	0
9.0– 9.4	2	1.5	4	50–54	1	1
9.5– 9.9	1	1.6	1	55–59	0	0
10.0–10.4	2	1.7	0	60–64	1	0
10.5–10.9	0	1.8	0	65–69	1	0
11.0–11.4	1	1.9	0	70–74	0	0
11.5–11.9	0	2.0	1	75–79	0	0

LOCATION

A. Single Diverticula	9	29.97%
At tip	3	9.99%
Along meso-appendix border	4	13.32%
Along antimeso-appendix border	1	3.33%
Perforated into meso-appendix	1	3.33%
B. Multiple Diverticula	21	69.93%
1. Only on meso-appendix border	7	23.31%
Only on antimeso-appendix border	3	9.99%
On both borders	5	16.65%
At tip and meso-appendix border	2	6.66%
At tip and antimeso-appendix border	4	13.32%
2. Perforated cases	5	16.65%
a. Along meso-appendix border	3	9.99%
b. Along antimeso-appendix border	2	6.66%

Figs. 1 to 6 depict characteristic findings in four of the cases of this series.

Approximately 60 per cent of these cases were associated with acute inflammation and 16.6 per cent had perforated which in three instances initiated pseudomyxoma peritonei. Seventy per cent of the specimens possessed multiple diverticula, while 43.3 per cent were situated on the meso-appendiceal border. Sixty-two point five per cent of all of the diverticula had a similar location. Eighty per cent of these cases occurred in individuals past 30 years of age. The average dimensions of the appendices were 7.86 by 1.18 cm. The length is within normal limits, but the diameter is approximately 3.0 Mm. greater than normal. The 30 graphic drawings show the common presence of abnormal degrees of lumen stenosis and of greatly thickened appendiceal walls. Both of these findings are indicative of previous acute inflammations

FIG. 1.—(Case 29.) Postmortem specimen. Base of the appendix. Inflammatory type of diverticulum. Note absence of muscularis in the walls of the diverticulum. It is this type which rapidly perforates in acute appendicitis. (×14½.)

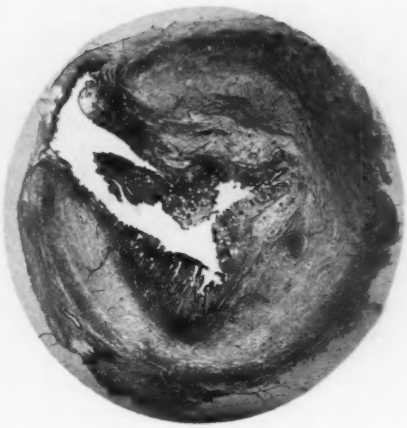


FIG. 2.—(Case 22.) Surgical specimen. Proximal third of the appendix: cross-section of the lumen showing a beginning acquired diverticulum which is penetrating the muscularis through a vascular hiatus. Note the hypertrophy of the muscularis which is a common finding in this type of diverticulum. (×6.) Courtesy of Dr. Albert F. Brown.)

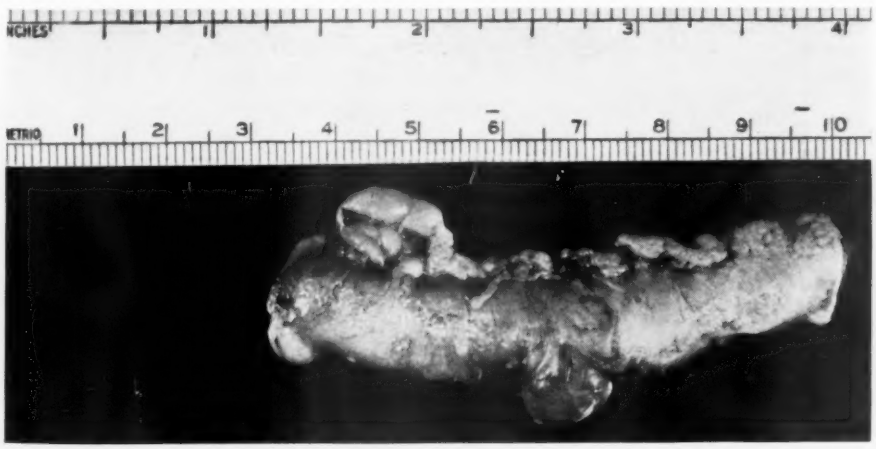


FIG. 3.—(Case 21.) Surgical specimen. Diverticula present at the tip and middle third of the appendix, on the antimeso-appendiceal border. Early acute appendicitis.

which were of considerable severity and produced marked narrowing or obliteration of the appendiceal lumen during the reparative processes of healing. This advanced degree of luminal narrowing was a most important causa-

FIG. 4.—(Case 21.) Surgical specimen. Cross-section through the large diverticulum in the middle of the appendix (Fig. 3). Typical acquired false inflammatory type of diverticulum showing acute, diffuse, ulcerative appendicitis. (×6.)

FIG. 5.—(Case 21.) Surgical specimen. Cross-section through the small diverticulum at the tip of the appendix (Fig. 3). Typical acquired false inflammatory type of diverticulum penetrating through the muscularis by a vascular hiatus. (×6.)

FIG. 6.—(Case 23.) Surgical specimen. Cross-sections of appendix showing two acquired diverticula associated with an early mucocele, in the middle third. Section taken through the base of the appendix shows obliteration of the lumen. Subacute appendicitis. (Courtesy of Dr. H. A. Waggener.)

tive factor in this condition. Most of the specimens revealed marked hypertrophy of the muscularis. Cases 6 and 9 had congenital true diverticula.

CONCLUSIONS

Diverticula of the vermiform appendix are of importance inasmuch as subsequent acute inflammation in such appendices presents atypical signs and symptoms that are commonly followed by early perforation with the frequent causation of either generalized peritonitis or pseudomyxoma peritonei. Thus, it is imperative that during the course of abdominal explorations the appendix be examined under direct vision to rule out the presence of appendiceal diverticula. If diyerticula are found, appendectomy should always be performed.

The literature upon this subject has been reviewed and the data derived from 60 previously reported cases have been tabulated. Thirty cases have been collected for study and their data have been summarized by means of tables and graphic drawings. A ready comparison is thus afforded between these two sources of material.

The incidence in this study was determined to be 0.77 per cent in 3,017 consecutive appendectomies and 0.66 per cent in 1,054 consecutive unselected postmortem appendices. Approximately 78 per cent of these cases were associated with varying degrees of acute inflammation at the time of their removal.

The great majority of instances were indirectly caused by a previous acute inflammation which in turn caused varying degrees of luminal atresia. The results and data obtained from this study are quite comparable with previously published studies.

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THE USE OF GLYCERYL TRINITRATE (NITROGLYCERIN) FOR THE CONTROL OF PAIN FOLLOWING CHOLECYSTECTOMY

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WE PREVIOUSLY have described an apparatus for measuring changes in pressure in the common bile duct.[1, 2] Observations on intrabiliary pressure were made in cases in which T tubes had been placed in the common bile duct at the time of operation, for the purpose of prolonged biliary drainage. Recurrent attacks of biliary pain following cholecystectomy were found to be associated with an increased intrabiliary pressure as high as 160 Mm. of water, while in the same case this pressure ordinarily varied between 0 and 20 Mm. of water. Subcutaneous administration of 1/6 grain (0.01 Gm.) of morphine produced an increase in the intrabiliary pressure which began two to five minutes after administration and reached a peak of 200 to 300 Mm. of water ten minutes later.

An increase in pressure was accompanied in some cases by severe attacks of pain similar to those from which the patient ordinarily suffered. Inhalation of amyl nitrite was found to produce an immediate decrease in the intrabiliary pressure to zero, with relief of the pain, which, however, returned after ten minutes. When 1/100 grain (0.0006 Gm.) of glyceryl trinitrate (nitroglycerin) was placed under the tongue it produced a moderate decrease in the pressure and effected relief of the pain five minutes after administration. The effect lasted at least one hour.

This report is concerned with the case histories of individuals who suffered from the postcholecystectomy syndrome and with the results of the use of glyceryl trinitrate for the relief of the pain.

CASE REPORTS

Case 1.—A white male, age 32, had suffered from repeated attacks of severe epigastric pain since his gallbladder had been removed nine years before he came to the Clinic. At intervals of days, weeks, or months he had had attacks of excruciating epigastric pain which had extended to the back. During the course of the attacks, which sometimes had lasted as long as 18 hours, he occasionally had taken as much as 12 grains (0.77 Gm.) of sodium amytal, a pint of whisky, and even inhalations of chloroform.

Physical examination was negative. Roentgenologic examination of the stomach, kidneys, ureters, and bladder did not reveal any abnormality.

Subcutaneous administration of 1/6 grain (0.01 Gm.) of morphine sulphate was followed in 15 minutes by an attack of excruciating epigastric pain. Inhalation of amyl

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nitrite produced immediate and complete relief. Pain returned in ten minutes, at which time 1/100 grain (0.0006 Gm.) of glyceryl trinitrate was placed under his tongue. This produced complete relief of pain in five minutes. Pain returned in one hour; this undoubtedly was attributable to the continued action of the morphine. While the patient was under our observation, administration of glyceryl trinitrate again relieved the pain. This time the pain did not return.

Laparotomy revealed the common bile duct dilated to twice the normal size. The common bile duct was opened and a small scoop was passed into the duodenum. No stones were found but a definite tug was experienced as the scoop passed the sphincter of Oddi. There was some thickening of the head of the pancreas. A T tube was inserted into the common bile duct for prolonged drainage. The postoperative course was uneventful and the patient was dismissed but was instructed to return later for removal of the T tube.

Case 2.—A nurse, age 27, had undergone a cholecystectomy because of attacks of pain in the right upper quadrant of the abdomen, accompanied by nausea and vomiting, a year and one-half before she came under our observation. The gallbladder had been found to be the site of a chronic inflammation but it had not contained any stones. The patient had been well until four months following the cholecystectomy, when a tight feeling had developed around the lower part of the thorax and she complained of pain at the right subcostal margin. It had been associated with vomiting which had continued for four hours. The pain had not been relieved by codeine which had been administered hypodermically. Residual soreness had remained for two days. There had not been any elevation of temperature at the time of this attack. During the year previous to her coming under our observation, she had had other similar attacks, which had forced her to stop work and go to bed. Administration of glyceryl trinitrate has produced prompt relief of the last three attacks and has permitted the patient to continue her work.

Case 3.—A woman, age 38, had undergone a cholecystectomy five years before she registered at the Clinic. Following this operation she had continued to have repeated attacks of pain in the right upper quadrant of the abdomen; the pain had extended to the back and had been associated with fever, and at times with jaundice. She volunteered the information that she had never been able to get complete relief during the attacks and that two and even three hypodermic injections of morphine had been administered without effect. Exploratory laparotomy had been performed on four different occasions but she had not obtained any relief. At the time of the last exploration, the common bile duct had been opened but no stones had been found. Prolonged biliary drainage had not been instituted.

On arrival at the Clinic she was seized with a severe attack of pain, which began at the ninth costal cartilage and extended around the right side to the back. Complete relief was obtained by the administration of 1/100 grain (0.0006 Gm.) of glyceryl trinitrate. Laparotomy revealed the common bile duct dilated to four times its normal size, but it did not contain any stones. The head of the pancreas was essentially normal. There was an associated cholangeitis and a hepatitis, Grade 3, on a basis of 4. A T tube was inserted into the common bile duct. The patient was comfortable following the operation. An injection of morphine produced the usual increase in intrabiliary pressure and a typical attack of biliary pain resulted.

Case 4.—A woman, age 48, was admitted to the Clinic May 12, 1936, because of jaundice, pruritus, and loss of weight. In 1929 she had begun to have repeated attacks of biliary colic with occasional jaundice. Her gallbladder had been removed in April, 1935. In October, 1935, indigestion, pruritus, and jaundice had returned and had continued until the present time. The value for the serum bilirubin was 19.36 mg. per 100 cc. The hippuric acid test revealed an excretion of 2.71 Gm. of hippuric acid and 1.83 Gm. of benzoic acid in the urine. While the patient was in hospital she was seized with pain in the right upper quadrant of the abdomen. This was relieved by

inhalation of amyl nitrite, after which the pain did not return. On May 19, 1936, a laparotomy disclosed a common bile duct enlarged to about 2.5 cm. in diameter. It contained a stone of equal diameter. There was some narrowing in the pancreatic portion of the duct, and some thickening of the head of the pancreas. The pancreatitis was considered to be Grade 3, on a basis of 4. The liver was brownish in color and showed hepatitis Grade 3+.

Case 5.—A woman, age 56, was admitted to the Clinic May 5, 1936, complaining of frequent attacks of vomiting. Twenty years previously she had suffered from attacks of biliary colic. Her gallbladder had been drained and 12 stones had been removed. Four years before she came under our observation her gallbladder had been removed. It contained a stone and one was also found in the common bile duct. Following this operation she had continued to have repeated attacks of pain in the right upper quadrant of the abdomen. During the past year these attacks had been replaced by a dull ache. Vomiting had been present for the past four years, but had become more severe during the last year. She had vomited bile stained fluid about half an hour after a meal. The results of physical examination were essentially negative. She had never been jaundiced. On May 11, 1936, she was given morphine, grain 1/6 (0.01 Gm.), as part of the preoperative medication. This was followed shortly by severe pain in the right upper abdominal quadrant. Inhalation of amyl nitrite gave prompt and complete relief. At operation the common bile duct was found to be about twice the normal size; it was opened and two black lozenge-shaped stones, each about 1.2 cm. in diameter, were removed. Following this it was possible to slip first a small scoop, then a large one, through the ampulla of Vater and into the duodenum. Her convalescence has been satisfactory.

Case 6.—A woman, age 37, registered at the Clinic June 1, 1935, because of persistent biliary and duodenal fistulae. In 1913 she had undergone a cholecystostomy for gallstones. In 1923, she began to have recurrent attacks of biliary colic every two to three months. The colic had been accompanied by chills, fever, vomiting, and sometimes by slight jaundice. Pain had extended around into the right scapular region. Two to three hypodermic injections of morphine had usually been necessary to secure relief. In January, 1935, cholecystectomy had been performed elsewhere and the gallbladder had been full of stones. The common bile duct had not been explored. On the tenth postoperative day food and bile had drained through the incision.

She was operated upon at the Clinic June 7, 1935. A duodenal fistula near the pyloric sphincter was closed and a pyloroplasty was performed. The common bile duct was slightly enlarged. It was explored but no stones were found. She made an uneventful convalescence. She returned on March 18, 1936, because she had had ten severe and many mild attacks of epigastric pain. These had occurred between 7 and 9 P.M. and lasted until ½ to ¾ of a grain (0.032 to 0.05 Gm.) of morphine was administered. Pain extended to the right shoulder. The pain had been exactly similar to that which had occurred before the removal of her gallbladder. The severe attacks had been followed by residual soreness, itching and jaundice; the stools had been of a light color for one or two weeks after the attack. There had not been any qualitative food distress.

On March 24, 1936, operation showed the gastroduodenostomy to be in excellent condition. Some narrowing of the common bile duct was noted in the region of the hepatic ducts. This was dilated. A T tube was inserted into the common duct and sutured. She made an uneventful convalescence. On the twenty-first postoperative day the intrabiliary pressure was 78 Mm. of water, much higher than the average pressure, which varies from 0 to 20 Mm. of water. Morphine, 1/6 grain (0.01 Gm.), was given subcutaneously. In two and one-half minutes the patient complained of a feeling of pressure in the right upper quadrant of the abdomen. She said that she felt like she did when an attack was about to begin. Eight minutes after administration of the morphine, she complained of severe pain in the right upper quadrant of the abdomen.

She felt "hot" all over and was nauseated, remarking that all of these symptoms had accompanied the regular attacks of pain. The intrabiliary pressure at this time was 140 Mm. of water. The T tube was disconnected from the apparatus in order to allow the bile to flow out freely. At the same time inhalation of amyl nitrite was given. These measures gave relief except for some residual soreness. On the following day choledochograms were taken in order to determine the cause of the persistent intrabiliary pressure. The roentgenogram revealed a spasm at the lower end of the common bile duct, at the level of the second lumbar vertebra (Fig. 1*a*). A second choledochogram, which was taken after 1/100 grain (0.0006 Gm.) of glyceryl trinitrate had been

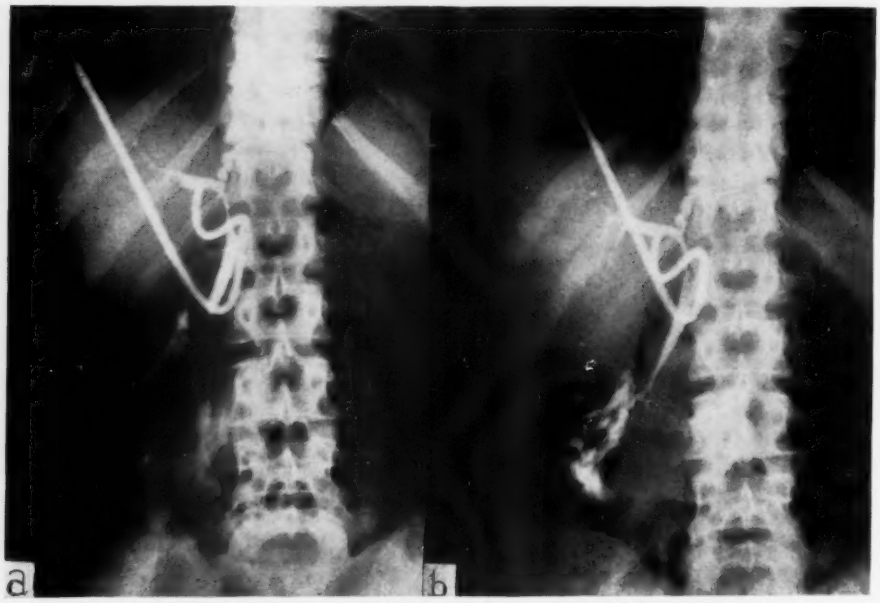

FIG. 1.—(a) Roentgenogram made following injection of brominol, showing obstruction at the lower end of the common bile duct at the level of the second lumbar vertebra. This patient had a persistent increase in pressure within the common bile duct to 70 Mm. of water (normal 0 to 20 Mm.) (b) Roentgenogram of same patient as shown in (a) and made with the same technic five minutes after administration of amyl nitrite. There is no evidence of spasm at its original site although there is some narrowing of the common bile duct below this point.

placed under the patient's tongue, revealed complete absence of any suggestion of a spasm, although it did reveal a very definite narrowing of the lower end of the common bile duct, opposite the third lumbar vertebra (Fig. 1*b*).

ADDITIONAL CASES

We will briefly mention six other cases in which the patients had attacks of biliary colic following removal of the gallbladder. In one case the patient was a woman; an attack of biliary colic was induced by the injection of 1/6 grain (0.01 Gm.) of morphine sulphate, given as part of the preoperative medication before a partial thyroidectomy. Inhalation of amyl nitrite effected relief for 15 minutes. In another case, a physician, an attack of biliary colic developed following the injection of 1/6 grain (0.01 Gm.) of morphine in connection with the extraction of a tooth. The attacks of pain from which this patient ordinarily suffered were severe enough to require ½ grain (0.032

Gm.) of morphine and incapacitated him for a day. On two occasions he had been able to relieve an attack of pain by taking glyceryl trinitrate. In a third case the patient was a woman who had her breast amputated at the Clinic. One grain (0.065 Gm.) of codeine, which was administered subcutaneously, produced an attack of biliary colic which lasted for several hours. The patient said that "hypodermics" previously had produced attacks of pain.

In three other instances pain occurred in the right upper quadrant of the abdomen during convalescence following cholecystectomy. In each the pain was promptly and completely relieved by administration of glyceryl trinitrate.

Administration of Glyceryl Trinitrate to Relieve Biliary Colic

We have observed relief of biliary colic by means of administration of glyceryl trinitrate in two cases in which the gallbladder was present at the time the drug was given. In one of these cases the patient was a woman, age 22, who complained of repeated attacks of pain in the right upper quadrant of the abdomen, which had occurred intermittently for two years. The roentgenogram revealed a gallbladder full of stones. We had the opportunity of observing her during an attack which continued for one and one-half hours in spite of the administration of two doses of morphine, each of which consisted of 1/6 grain (0.01 Gm.). Forty-five minutes after administration of the second dose of morphine, inhalation of amyl nitrite produced immediate relief of pain. It returned ten minutes later, at which time 1/100 grain (0.0006 Gm.) of glyceryl trinitrate, placed under the tongue, produced complete relief in two and one-half minutes. Pain returned in one hour, undoubtedly as the result of the continued action of morphine. A second dose of glyceryl trinitrate produced complete and permanent relief. She was later operated upon and a gallbladder full of stones was removed. The common bile duct was normal in size and color, and no stones could be felt in it, so it was not opened.

In the other case, a man, age 66, had suffered from repeated attacks of biliary colic, accompanied by gaseous eructations, nausea, and light colored stools. Because of the presence of bronchial asthma and a definite pulmonary emphysema, an operation was considered inadvisable. Glyceryl trinitrate was prescribed for the relief of the pain. He reported prompt and complete relief. In this instance the possibility of angina pectoris must be considered, although the history was typical of biliary colic.

Comment.—The data which we have collected on the subject suggests that administration of morphine is likely to precipitate an attack of biliary colic. Administration of 1/6 grain (0.01 Gm.) of morphine in such cases will frequently produce an increase of intrabiliary pressure to 160 to 300 Mm. of water for two or more hours, accompanied by severe pain. While a large dose of morphine will decrease the patient's sensibility to pain by acting on the higher nerve centers, it, at the same time, prolongs and even augments the increase in pressure in the common bile duct. Patients who have disease of the gallbladder frequently say that morphine gives them a feeling of fulness

or makes them sick. The explanation probably is that a normally functioning gallbladder can maintain intrabiliary pressure at a normal level by absorption of fluids and relaxation of its smooth muscle, while a diseased gallbladder, on the other hand, does not possess this function. We suggest the use of morphine as a diagnostic procedure in the study of patients who have the postcholecystectomy syndrome. If administration of morphine brings on an attack of pain and glyceryl trinitrate relieves it, the evidence is in favor of the condition being the result of a disturbance in the sphincteric mechanism at the lower end of the common bile duct either with or without associated stones in the common bile duct. Administration of glyceryl trinitrate, in doses of 1/100 grain (0.0006 Gm.), will relieve the pain associated with the postcholecystectomy syndrome. We do not recommend its use, except as a temporary measure until after the common bile duct has been explored, since stones in the common duct may account for the sphincteric spasm.

We have not seen any untoward effects from the use of glyceryl trinitrate, except a feeling of warmth, weakness, and occasionally a tightness in the head. These are very transitory, however, and pass off in a few minutes. However, we recommend that the patient be in the recumbent position when the drug is taken. We have found that the tablets made for hypodermic use are more effective than the regular triturates.

SUMMARY

We have reported a series of nine cases in which repeated attacks of biliary colic developed after the gallbladder had been removed. In these cases, subcutaneous injection of 1/6 grain (0.01 Gm.) of morphine sulphate produced pain, which was completely relieved by administration, under the tongue, of 1/100 grain (0.0006 Gm.) of glyceryl trinitrate, or by inhalation of amyl nitrite. In two of these cases stones were subsequently found in the common bile duct at operation.

We have mentioned two cases in which pain, which was associated with biliary colic and which occurred before cholecystectomy, was relieved by administration of glyceryl trinitrate. In three other cases the patients were relieved of similar attacks which occurred shortly after cholecystectomy.

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AN OPERATIVE PROCEDURE FOR RIGHT-SIDED ULCERATIVE ILEOCOLITIS

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ULCERATIVE colitis frequently commences in the ascending (right-sided colitis) or in the transverse colon. When it originates in the right side of the colon, it extends backward to the caput coli and through the ileocecal valve into the ileum, and also forward into the transverse, descending and sigmoid colon. When the disease commences in the transverse colon, it likewise extends in both directions, *i.e.*, backward towards the cecum and into the ileum, and forward into the descending colon and sigmoid. When the ileum becomes involved, we have termed the condition ulcerative colo-ileitis to indicate that the disease originates in the colon and extends subsequently into the ileum.

The sigmoid flexure and rectum in these cases of right-sided and transverse colitis are involved only in the very late stages of the disease. Sigmoidoscopy will usually show the sigmoid and rectum to be uninvolved. This is confirmed by roentgenologic examination which shows the sigmoid to be ballooned out to retain its normal haustrations.

In the severe cases of right-sided and transverse colitis, those that have resisted all forms and types of medical treatment, it has been the practice of some surgeons to establish an ileostomy in order to exclude the entire colon from the fecal stream and thus put the colon at rest; others perform an ileosigmoidostomy with the same object in view, but ileosigmoidostomy surely does not put the colon at rest or divert the feces from the diseased colon because retrograde peristalsis carries the fecal material from the site of implantation of the ileum into the upper portions of the colon.

Ileostomy does not afford the opportunity to irrigate and to cleanse the diseased colon. Besides, it has the additional disadvantage of delivering fluid fecal material onto the abdominal wall and thus is an additional serious source of infection if further operative procedure upon the diseased colon is to be carried out.

In order to put the diseased colon completely at rest and in order to irrigate and cleanse it thoroughly, I have, in five cases, carried out the following procedure: A left-sided transrectus incision is made extending three or four inches upward from the symphysis; the terminal ileum is identified and delivered out of the wound. The healthy sigmoid is similarly recognized and delivered into the abdominal wound. The healthy ileum, as near to the ileocecal valve as is possible, is cut completely across and its mesentery divided. Both ends are closed by two or three tiers of sutures (Fig. 1), an inner chromic catgut through all the coats, reinforced by one or two layers of interrupted linen or chromic catgut sutures. The proximal end of the ileum

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is now joined to the lower sigmoid just above the peritoneal reflection by a side-to-side anastomosis. Several inches above this side-to-side anastomosis the sigmoid is cut completely across, the distal end closed by a row of chromic catgut sutures reinforced by one or two layers of linen or catgut, and the

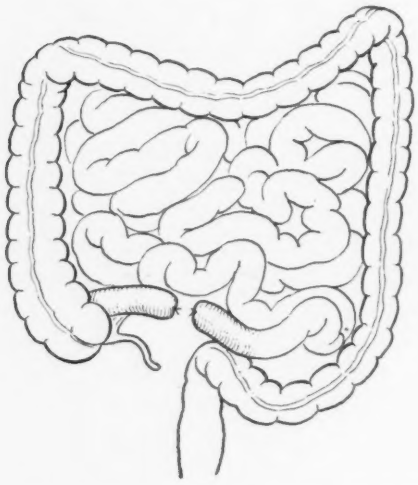

FIG. 1.—Division and closure of both ends of the terminal ileum above the site of disease.

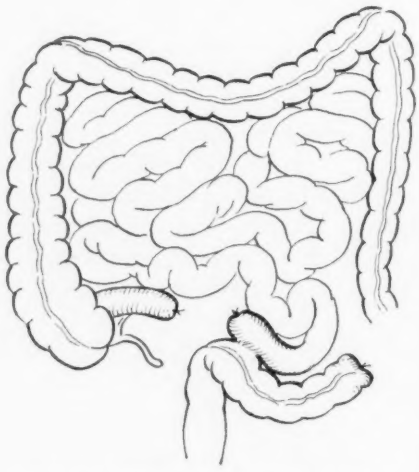

FIG. 2.—Implantation of proximal end of ileum into the lower sigmoid. Complete division of two upper ends of sigmoid. Closure of the distal end of sigmoid. Establishment of artificial anus in proximal end of sigmoid.

proximal end tied off with a heavy silk suture, thoroughly carbolized and brought out through the upper angle of the wound (Fig. 2). The rest of the abdominal wound is closed in layers. The heavy silk suture around the proximal end of the sigmoid is left in situ for 48 to 72 hours and then removed, leaving a fistula in the proximal end of the sigmoid (Fig. 3). The fecal stream is thus entirely diverted into the lowermost sigmoid and rectum, and the fistula in the sigmoid permits the free drainage of the products of inflammation from the diseased colon. After 10 to 14 days, the colon is irrigated through the sigmoidal fistula.

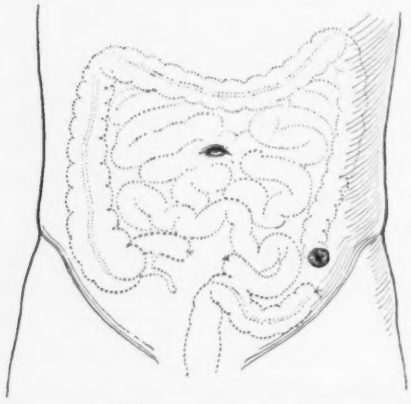

FIG. 3.—Artificial anus of proximal end of sigmoid.

In two cases the entire colon and the diseased portion of the ileum have been subsequently removed.

CASE REPORTS

Case 1.—Male, age 20, referred by Doctor Crohn. He had an ulcerative colitis which commenced in the proximal portion of the transverse colon. While under observation and treatment, the disease had extended backward into the caput coli and through the ileocecal valve into the ileum. It had also extended forward through the whole of

the transverse colon and up into the upper third of the descending colon where it had stopped abruptly. The lower half of the descending colon and sigmoid were entirely normal.

At the time of examination, he was very sick. The disease had resisted all forms of treatment. He was having temperatures between 102° and 104° F.; had a profuse bloody, purulent diarrhea and had lost a great deal of weight. After repeated transfusions, the above described operative procedure was carried out.

Within 48 hours after the operation, the temperature became normal and his general condition began to improve. He was discharged from the hospital after three

FIG. 4.—Ulcerative colitis involving the ascending and transverse colon and extending into the terminal ileum.

weeks, with normal temperature, discharging considerable pus and blood through the sigmoidal fistula, and having but three or four normal fluid stools daily.

Four months after this first operation, the diseased terminal ileum, the whole ascending, transverse, descending colon and sigmoid down to and including the fistula were removed at one operation. He made an uninterrupted convalescence and was discharged four weeks after operation. He is gaining rapidly in weight, has usually three normal semisolid movements a day; appetite is good. His blood examination was practically normal (Fig. 4).

Case 2.—A young lady came under observation 14 years ago, suffering from a very severe ulcerative colitis which involved the caput coli and the ascending colon. For several years after the onset of her disease, there were periods during which she was very ill with high temperature and profuse, bloody, purulent diarrhea. During one of these exacerbations, an appendicostomy was performed by Dr. Joseph Blake, with the idea of irrigating the diseased colon.

This operation gave her no relief. She continued to have severe, bloody, purulent diarrhea and at times severe recrudescences of fever lasting for many weeks. About four years after the establishment of this appendicocecostomy, the patient demanded that

FIG. 5.—Ulcerative colitis involving sigmoid and colon and extending into the terminal ileum.

the artificial opening be closed, it having become a source of great annoyance, constantly giving rise to infections of the abdominal wall around the site of the fistula and apparently affording no benefit.

Upon opening the abdomen with the intention of closing the fistula, the caput coli was found thickened and indurated and had lost all of its elasticity. The terminal ileum was healthy. The fistulous opening in the cecum was closed by a plastic procedure. This remained closed for two months when the suture line broke down and the fistula was reestablished.

For the next three years the course of the disease was about the same. The recrudescences of high temperature and the continuous bloody, purulent diarrhea persisted. A second attempt was made to close the fistula, at which operation the terminal ileum was found to be normal; the caput coli, however, had become even more rigid and leathery. By removing the mucosa and the submucosa of the wall of the cecum adjacent to the fistula, enough soft and elastic cecal wall was secured to effect closure of the opening. A satisfactory result was obtained for a period of three months when the suture line again broke down, resulting in the reformation of the fistula.

The disease again continued in its severe course with intermissions of comparative well being, but the severe, bloody, purulent diarrhea continued. At times, the large joints became swollen and were markedly inflamed and attacks of iritis seriously threatened her eyesight.

In November, 1935, the patient was in poor condition and the question of radical removal of the diseased colon was considered. Sigmoidoscopy showed the rectum and lowermost sigmoid comparatively uninvolved. There were some small superficial ulcerations of the mucous membrane in the lower sigmoid but no polyposis. Roentgenologic examination demonstrated the rectum and lowermost sigmoid to be elastic and ballooned out.

The procedure previously detailed was carried out, *i.e.*, ileosigmoidostomy just above the peritoneal reflection, closure of the distal end of the ileum, division of the sigmoid, closure of the distal end of the sigmoid and establishment of a sigmoidal colostomy. Her course after this operation was encouraging. Her stools became free of blood and pus, there being about four to five fluid semisolid movements a day. Through the sigmoidal colostomy, however, as much as eight to 15 ounces of purulent, bloody material were discharged every 24 hours. Her general condition improved and her temperature remained normal. All joint and eye lesions disappeared.

After four months the terminal ileum, which had become very much diseased, was removed as well as the ascending and proximal half of the transverse colon (Fig. 5). Her general condition contraindicated the complete removal of the colon. At the present time her general condition is very much improved. She has about three to four semisolid movements a day, normal in character. The fistula in the sigmoid discharges about five drops of purulent material in 24 hours. The remaining portion of the colon will be removed subsequently.

The other three cases operated upon according to this method have not had the colon removed as yet. One is that of a boy desperately ill and delirious with high temperature, who improved immediately after operation. Another one, a case of polypoid colitis, is awaiting colectomy. The third one has improved so much and has so little discharge from the diseased colon through the sigmoidal colostomy, that she is debating the necessity of having the diseased colon removed.

CONCLUSIONS

By this procedure, one is enabled, first of all, to put the diseased colon completely at rest.

An outlet is afforded for the blood, pus and other products of inflammatory reaction.

Cleansing of the diseased colon by irrigating fluids can be readily carried out.

Where a colectomy is contemplated, its dangers are not increased by the presence of a discharging ileostomy wound.

The procedure is not attended with much shock, and as seen in our cases, can be tolerated even during the severe exacerbations of the disease.

THE SURGICAL TREATMENT OF FIVE HUNDRED HERNIAE

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THE surgical treatment of hernia has now progressed to the extent that in the absence of complications such as strangulation, it is attended by practically no mortality. The results have become increasingly satisfactory. Occasional recurrences, however, are encountered, and this, together with the fact that herniae of various types constitute the second most frequent lesion encountered on a general surgical service, makes careful analyses of groups of cases worthwhile in evaluating the procedure employed and perhaps in indicating where other methods would have been preferable. An analysis of 500 consecutive cases is therefore presented, including 367 inguinal, 34 umbilical, 33 femoral, 18 epigastric, and 48 postoperative ventral herniae. Each type was treated by the same or similar operative procedure, and the technic in all types included the use of silk as a suture material.

Many factors may, of course, influence the adequacy of the repair of a hernia, but not the least of these is the condition of the structures which must be utilized in the repair. Their condition may in turn depend upon a number of circumstances such as the muscular development, the age of the patient and his general state of health. Of all of these, however, the most important single factor is the duration of the hernia, and for this reason operation should be undertaken as soon as possible after the hernia is recognized.

An effort has been made to reduce the incidence of infections and postoperative pulmonary complications which contribute to the poor results and the mortality in hernial operations by the adherence to detail of procedure. There were no deaths in this series of cases, few infections and no serious pulmonary complications.

General Technic.—The preoperative treatment of hernia is not distinctive save in obese patients in whom respiration and circulation may be embarrassed by the return of hernial contents to the abdominal cavity. Such a case is prepared for operation by spending from two to seven days in bed with a tight binder applied to the abdomen. Catharsis is freely administered and a liquid diet is given for the purpose of decompressing the intestinal tract. An extremely obese patient is advised to reduce before surgical treatment is undertaken, unless postponement is contraindicated.

Anesthesia.—We prefer local anesthesia in hernia operations, mainly for two reasons: (a) postoperative pulmonary complications appear to be less frequent; (b) nausea and retching, which place an extra strain upon the wound, are less severe. The opinion held by some that the injection of a local anesthetic leads to infection is not borne out by our experience in this series of cases, as there were no deep infections.

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The details of the operative procedure will be discussed under the several headings. In all hernia cases the field is prepared with care to avoid contamination from unprepared areas. The dissection is carried out with a sharp instrument, bleeding vessels are ligated with meticulous care, using silk ligatures. The wound is repaired with interrupted silk sutures, except when infection is present.

Postoperative Care.—All patients operated upon for hernia are kept in bed for 14 days unless the hernia has been large or the structures of less than usual strength, when the period in bed may be prolonged.

Inguinal Hernia.—In the group of 367 inguinal herniae there were 303 indirect, 38 direct, and 26 recurrent herniae. Three hundred and six operations were performed under local, 45 under general and 16 under spinal anesthesia.

Indirect Inguinal Hernia.—In repairing an indirect inguinal hernia, we use one of two methods. If the structures are strong and the defect small, a Halsted[1] repair without transplantation of the cord is done. In this procedure, the sac is dissected up to its neck, where it is ligated and transfixed with doubled silk. The stump retracts behind the internal oblique muscle. The cremaster muscle and fascia are drawn up under the edge of the conjoined tendon and internal oblique muscle in an effort to partially obliterate the inguinal canal. The edges of the internal oblique muscle and conjoined tendon are sutured to Poupart's ligament, the cord being closely embraced by these structures as it emerges. The margin of the lateral portion of the external oblique is then secured beneath the mesial portion by a series of mattress sutures and the mesial portion of the external oblique is brought to overlap this laterally and secured in a similar manner. The sutures throughout this procedure are interrupted and of black silk.

If the structures are weak or if the defect is large, a Halsted repair with transplantation of the cord to the subcutaneous tissue is done. This is the procedure with which the term Halsted hernial repair is most commonly associated. All the muscular and fascial layers are united beneath the cord. This obliterates completely the old external ring and makes a new one, which, although opposite the internal ring, tends to permit recurrences less frequently.

Two points concerning technic are emphasized: (a) sutures should not be drawn so tightly as to interfere with the circulation in the tissue and thus weaken the repair; (b) approximation of the structures should be accomplished without undue tension after adequate mobilization so as to permit the newly constructed abdominal wall to heal without separation.

Seventeen of the 303 indirect inguinal herniae required immediate operation because of incarceration or strangulation. Two hundred and fifty-three of these patients have been studied in the Follow Up Clinic and of these, six have not been cured by operation, an incidence of recurrence of 2.37 per cent.

Direct Inguinal Hernia.—Indirect inguinal herniae, for the most part, develop because of a congenital weakness brought about by the descent of the testicle into the scrotum, whereas the direct herniae occur because of an

acquired attenuation of the structures comprising the conjoined tendon. In these latter, therefore, to overcome the weakness of the abdominal wall, a repair with transplantation of the cord is more frequently necessary.

Thirty-two of the 38 patients have been studied in the Follow Up Clinic and of these two showed evidence of recurrence, an incidence of 6.21 per cent.

Recurrent Inguinal Hernia.—The 26 patients in this group had been operated upon elsewhere, from one to four times, previous to their admission to this clinic. The usual technic we employed was that of Halsted with transplantation of the cord to the subcutaneous tissues. All recurrences occurred in direct herniae in five of which the cord was transplanted and one in which transplantation was omitted in the repair. Twenty of the 26 patients have been observed in the Follow Up Clinic, of which six cases or 30 per cent had recurrences.

It has been suggested by Gallie[2] that large fascial transplants be used to fill the defect where structures cannot be readily approximated. In his series of cases there were recurrences in only 10 per cent. His method will be tried here in the future in the hope that the incidence of recurrences may be lowered.

Femoral Hernia.—In the group of 33 femoral herniae there were 19 on the right side. This predominance on the right has been observed by others. Thirty of these patients were female, three were male. Ten cases required immediate operation; five for incarceration and five for strangulation. The procedure was carried out through an inguinal incision and the sac exposed below Poupart's ligament. The external oblique fascia and the peritoneum were then divided, and the hernia and its contents reduced. The neck of the sac was inverted and closed. The femoral ring was then obliterated in the classic manner, employing silk sutures to approximate the pectineus fascia and Poupart's ligament.

Twenty-six of the cases in this group were studied in the Follow Up Clinic. There were three recurrences, an incidence of 11.1 per cent. One case had been operated upon in the fourth month of pregnancy and recurred soon after delivery, while another had worn a truss for 16 years prior to operation. In the third there was no evident cause for recurrence.

The fact that femoral hernia occurs more frequently in later life is borne out by this series, in which 27 of the 33 patients were over 40 years of age. The incidence of incarceration and strangulation was higher in this type than any other. Ten or 30 per cent of these were acute herniae. The age incidence and the frequency of intestinal obstruction in this group explains the higher mortality generally associated with it. For example, it was necessary to operate for a strangulated femoral hernia in a woman over 80 years of age who had had intestinal obstruction for almost 48 hours.

Umbilical Hernia.—Twenty of the 34 cases in this group were markedly obese. The hernia had persisted for long periods of time in the majority of instances but was not associated with serious symptoms. The size of the hernial ring was moderate except in the three recurrent umbilical herniae in which it was very large. Nine cases were acute, five requiring immediate

operation for incarceration and four for strangulation. The majority of these herniae were repaired by the method advocated by Blake,[3] which consists of the longitudinal overlapping of fascia of the recti utilizing the anterior and posterior sheaths when possible. In three cases a Mayo[4] repair was done. The anesthetic employed was local in 20 cases, general in ten and local supplemented by general in four. Twenty-eight of the 34 patients have been seen in the Follow Up Clinic; no recurrences have been observed.

Epigastric Hernia.—These herniae occurred above the level of the umbilicus and were small; some were multiple. Two patients required immediate operation, one for strangulation and the other for incarceration. Contrary to the opinion frequently held—that the epigastric hernia is often asymptomatic—these patients without exception gave symptoms of abdominal pain and discomfort. In two cases repair had been previously attempted. The method of repair was the same as in umbilical herniae. Fourteen of this group of cases have been followed; two (14.2 per cent) were not cured by operation. In one instance the patient was very obese and uncooperative; in the other the hernia had recurred previously.

Postoperative Ventral Hernia.—There were 48 ventral herniae in the series. In 12 cases the defect in the abdominal wall followed cholecystectomy, 16 followed drained appendectomy wounds and 20 occurred in lower midline incisions for pelvic operations. Six of the 48 herniae were recurrences. Twenty patients were over 50 years of age; 33 were definitely obese. Five of the ventral herniae were acute and four of the patients were poor operative risks. In no case was intestine resected.

Reference has been made to the preoperative treatment given this group of patients. The peritoneum was opened in every case. We believe that careful closure of the peritoneum and overlapping of the fascia over it lends strength to the repair of the wound. As in other repairs, silk sutures were used without exception. There was one superficial wound infection in this group.

The anesthesia employed was general in 15; local in 23; spinal in six; and local supplemented by general in four.

All but seven of the 48 cases have been reexamined in the Follow Up Clinic. There were no recurrences. The seven patients who failed to return to the Follow Up Clinic reported by letter or telephone that they were well.

"Acute" Hernia.—In a recent analysis of a series of herniae treated at St. Vincent's Hospital (New York) O'Shea[5] uses the term "acute" hernia to denote cases which required immediate operation. We employ this term to designate herniae in which there was incarceration or strangulation. An incarcerated hernia is not always considered an emergency, but immediate operation to rule out the possibility of strangulation is often indicated, as the transition from incarceration to strangulation and intestinal obstruction occurs too frequently to be disregarded. There were 56 acute herniae in this series; 30 were inguinal, ten femoral, nine umbilical, two epigastric and five postoperative ventral herniae. The bowel was found to be partially or completely obstructed in 19 instances.

It has been our policy first to relieve the intestinal obstruction in these patients. If the bowel is sufficiently viable it is returned to the abdominal cavity and the defect repaired. In femoral and inguinal herniae, if the bowel is gangrenous and resection is indicated, another abdominal incision is made and the bowel approached through it. A resection and anastomosis is performed or the bowel is merely brought to the surface of the abdominal wall, postponing the intestinal anastomosis until later.

That there were no fatalities in the acute herniae may, in part, be due to the plan of not imposing upon the patient, who is in poor condition, any procedure that may be done subsequently. A policy of early operation in hernia may in time eliminate entirely the mortality in these cases.

Postoperative Complications.—Immediate postoperative complications were noted in 27 cases. They appeared to have little relationship to the preoperative condition or age of the patient, nor to the type of hernia or to the method of repair. Only three patients had postoperative pulmonary complications. In one of these, a lobar pneumonia occurred on the first postoperative day; however, it prolonged the usual period in bed by only three days; the other two cases were of a less serious nature. The low incidence of pulmonary complications was, in our opinion, due to the extensive use of local anesthesia.

There were seven cases of phlebitis of the lower extremities, two of these occurred in the extremity on the side opposite the operation. One had multiple pulmonary infarcts which prolonged her stay in bed to 45 days. In nine cases the wound became infected, exclusive of those known to be grossly infected at the time of operation. The infection was, fortunately, superficial in all nine instances and in none did it involve the fascial layer of the wound. There was one superficial slough associated with the repair: a large postoperative ventral hernia in which the skin had been too closely undercut. Hematomata of the cord were noted six times and in one case the clot was so large that, to evacuate it, the wound had to be reopened. One patient had a coronary occlusion from which he recovered.

Follow Up.—The late results presented in this paper are based upon observations made in the Surgical Follow Up Clinic. Hernia patients are requested to return to the clinic for observation at six month intervals; the majority are glad to cooperate. Telephone calls and letters are not considered in the evaluation of end-results. Each patient is examined by at least one

TABLE I

SUMMARY OF RESULTS IN FIVE HUNDRED HERNIA OPERATIONS

	Total Number of Cases	No. Examined in Follow Up Clinic	Number of Recurrences	Percentage of Recurrence
Indirect inguinal.....	303	253	6	2.37%
Direct inguinal.....	38	32	2	6.21%
Recurrent inguinal....	26	20	6	30. %
Femoral.....	33	26	3	11.5 %
Umbilical.....	34	28	0	0
Epigastric.....	18	14	2	14.2 %
Postoperative ventral .	48	41	0	0

surgeon other than the operator. The study includes a careful evaluation of the result of the repair and the determination of complaints and symptoms which might point to a recurrence or the presence of complications. By this means 83.2 per cent of the 500 cases have been followed from six to 24 months after operation (Table I).

A review of the literature shows that it is generally conceded that from 65 to 75 per cent of all recurrences are evident within six months after operation. Thus Erdman[6, 7] states that 48 per cent of the recurrences in a large series of herniae took place within six months of operation and 80 per cent within a year. Masson,[8, 9] at the Mayo Clinic, found that 73 per cent of the herniae which recurred did so within six months, and 84 per cent within one year after surgical repair. A report from the Brooklyn Naval Hospital[10] shows that 65 per cent of all recurrences appeared within the first year after operation. Other reports[11] (Gibson and Felter,[12] Foss and Hicken,[13] and R. French),[14] offer similar figures.

CONCLUSIONS

(1) Five hundred consecutive herniae are reported, with brief descriptions of the therapy, and a careful study of the postoperative complications and the late results.

(2) It appears that with meticulous care, in every detail of the procedure, the incidence of infection may be lowered. It is also believed that local anesthesia decreases the number of postoperative pulmonary complications.

(3) In two types of herniae of this series, *i.e.*, the recurrent inguinal and femoral herniae, the incidence of recurrence is high.

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THE INTRAPERITONEAL APPROACH FOR REPAIR OF INGUINAL HERNIA*

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THE facility of an operation for the repair of inguinal hernia depends not only on the type and size of the hernia but also on adequate exposure of the structures involved. Large sliding herniae and some strangulated herniae with small, indurated rings require the best exposure obtainable. The importance of high ligation of the hernial sac is generally admitted. Increasing attention is being given to the transversalis fascia and to restoration of the internal ring.[1, 2, 3, 4] Study of 100 cases in which the intraperitoneal approach was used suggests that better exposure of the internal ring is provided by this method and that it has value in some of the unusual or difficult herniae.

The intraperitoneal approach, as described by La Roque,[5] exposes the internal ring from both the inner and outer aspects. It requires no different or additional skin incision and does not dictate the type of repair to be employed. The essential difference between the intraperitoneal and the usual approach is the addition of a muscle-split and peritoneal incision just above the internal ring. The neck of the sac may be removed and the internal ring repaired without danger to adjacent structures. The method of La Roque, slightly modified, was used in this series.

The idea of attacking the hernia from within is not new. It was suggested by Annandale[6] in 1876, by Tait[7] in 1883, and more recently by Jaboulay,[8] Leriche,[9] La Roque,[5] Soresi,[10] Banerjee,[11] Easton[12] and others. Some of the methods described call for additional skin incisions while others rely upon closure of the sac from the inner aspect without repair of the inguinal canal.

Technic of the Intraperitoneal Approach.—The skin incision is the one ordinarily used for operation on inguinal hernia. The aponeurosis of the external oblique is opened as usual and reflected to expose the internal oblique. The cremaster is seen masking the spermatic cord. The site for muscle-split is now selected. This is usually about one inch above the lower edge of the internal oblique (Fig. 1). This edge can be more readily felt than seen if the cremaster is well developed or if much fat is present. The muscle is then split parallel to its fibers and retracted to expose the transversalis fascia just above the internal ring (Fig. 2). The transversalis fascia and peritoneum are then incised as for appendectomy though at a somewhat lower level. The peritoneal cavity is now open at a point a little more than half an inch above the internal ring (Fig. 3).

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Up to this point the procedure has been that of an hernial incision to which a muscle-split has been added. The opening in the muscle is now gently

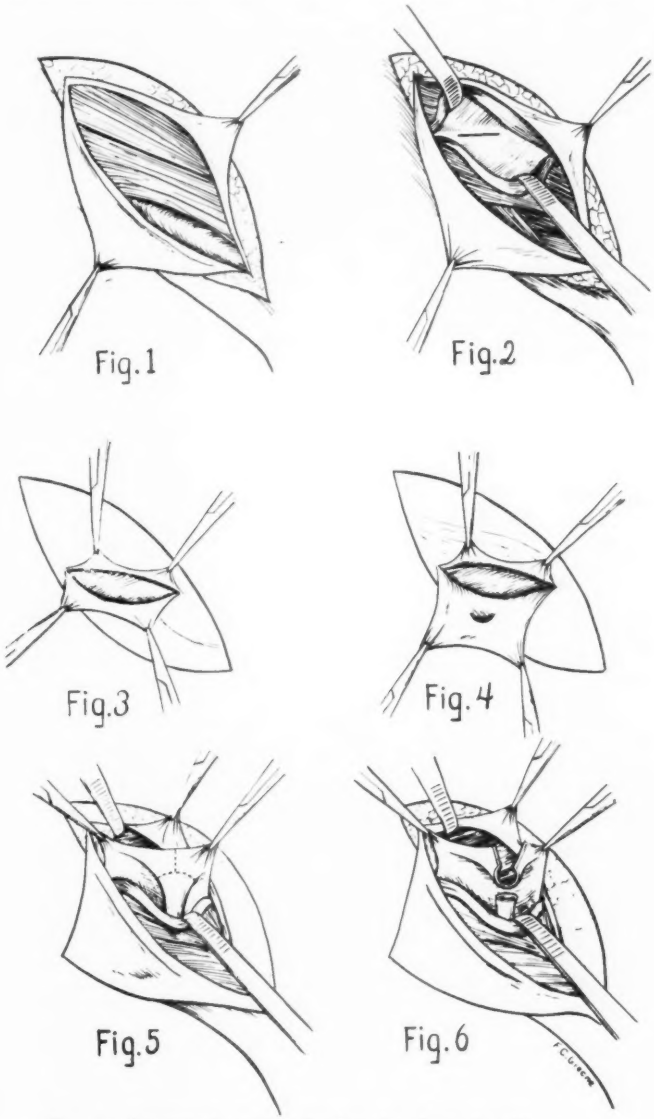

FIG. 1.—Aponeurosis opened showing site of muscle-split.
FIG. 2.—Muscle retracted showing incision in transversalis fascia and peritoneum.
FIG. 3.—Peritoneum open above internal ring.
FIG. 4.—Lower peritoneal flap rolled out to show inner opening of indirect sac.
FIG. 5.—Neck of sac dissected free—dotted line indicates incision around it.
FIG. 6.—Peritoneum ready for closure after excising neck of sac.

retracted downward while the lower edge of the incised peritoneum is grasped and pulled outward. With a little blunt dissection this lower peritoneal flap is mobilized so that the abdominal opening of an indirect sac will roll

into view (Fig. 4). If a sac is found its interior is explored with the finger or an instrument. Contents are liberated and reduced into the abdomen. Adherent omentum is cut between ligatures and the adherent portion is left in the sac. If intestine is adherent in the sac its separation is delayed until the neck of the sac is opened, when it can be done under direct vision. If adhesions to the parietal peritoneum of the inguinal region are found they are divided.

The sites of possible direct and femoral herniae are now palpated from within the abdomen. In children the opposite inguinal region can often be reached by the exploring finger. If a direct or femoral hernia is found I prefer to lift the cord and open the peritoneum through the posterior wall of the inguinal canal.

The next step is dissection of the neck of the sac. The index finger is passed into the abdominal opening of the sac while traction is made on the lower peritoneal flap by an instrument held in the palm of the same hand. The neck of the sac is now freed by blunt dissection, pushing the fat away from the outside of the peritoneum in the place between the peritoneum and transversalis fascia. Sharp dissection may be needed at the medial side of the neck of the sac where transversalis fascia is firmly adherent. The cord structures are somewhat separated as they enter the canal. The vas deferens should be identified and guarded. The inferior epigastric vessels lie just medial to the vas deferens. As the neck of the sac is freed it will be drawn up into the wound (Fig. 5).

When the neck of the sac is entirely liberated from surrounding structures the peritoneum is slit from the original opening down to and around the neck of the sac. The sac is no longer continuous with the parietal peritoneum (Fig. 6). The sac may be dissected out and removed or part of it left if its bulk will not interfere with proper repair. The lower edge of parietal peritoneum, where the neck of the sac was excised, is further mobilized by blunt dissection, pulled upward and sutured to the upper edge of the original peritoneal opening. This line of closure may be fixed at a higher level if desired, by mobilizing the upper peritoneal edge before suturing. If adhesions have been separated inside the internal ring the damaged parietal peritoneum should be removed before closure. This insures smooth peritoneum at the internal ring and leaves no raw surface for the formation of adhesions.

Reconstruction of the internal ring is an important step in the repair. The transversalis fascia may be thin but it usually can be found when one becomes familiar with it as seen from this aspect. This layer should be sutured with reasonable snugness around the cord structures, taking care to avoid injury to the vessels and vas deferens. From this point on the repair may be done according to the choice of the operator. If desired, the muscle-split and peritoneal opening may be closed after the canal has been repaired.

In this series preference was given to the fascial type of repair, with imbrication of the aponeurosis of the external oblique beneath the cord. Sharp

dissection was used as far as possible and tissues were handled gently with careful retraction. Fine needles and fine absorbable sutures were used. An attempt was made to avoid tight sutures and tension on suture lines. Special attention was given to hemostasis and elimination of dead space. Plain double 0 catgut was used for ligatures. On most of the bilateral cases two operators worked simultaneously. The average patient was kept in bed for two weeks, those with fascial transplants for three weeks.

TABLE I

HISTORY AND OPERATIVE FINDINGS IN 100 INGUINAL HERNIAE

Age—over 50	13 per cent	Medium sac	30 per cent
Age—under 20	9 per cent	Small sac	27 per cent
Truss worn	17 per cent	Large sac	43 per cent
Indirect	87 per cent	Sliding	5 per cent
Direct	13 per cent	Recurrent	2 per cent
Bilateral	15 per cent	Strangulated	4 per cent

Observations.—The operative findings in this series of 100 cases in which the intraperitoneal approach was used are summarized in Table I. All but two were ward patients. Some of them were undernourished, but all were in good general condition at the time of operation. Seventy-eight per cent of the patients were between 20 and 50 years of age. Ninety-one per cent of the cases were followed for one and a half years. At the end of two years only 82 per cent could be located for examination.

TABLE II

TYPE OF REPAIR AND RESULTS

Modified Andrews	69 per cent	Deaths	0 per cent
Bassini or Ferguson	31 per cent	Wound infections	1 per cent
Cord transplanted	79 per cent	Recurrence known	2 per cent
Cord not transplanted	21 per cent	Examined after two years	82 per cent
Fascial transplant	12 per cent	Fever* reaction (days)	3.4

* Rectal temperature of 100 degrees or over.

The type of repair used and results obtained are shown in Table II. The incidence of postoperative pain, abdominal distention and urinary retention did not appear to be greater than after the usual operation. One wound was infected with staphylococcus aureus but the infection responded promptly to the Carrel-Dakin technic. There was no recurrence in this patient after two years. No evidence of nerve or muscle injury was seen in any case. Tissue destruction as indicated by postoperative fever and wound reaction did not seem to be increased. There were five respiratory infections in this series which raised the average number of days of postoperative fever (100 degrees or over, rectal) to 3.4. For the remaining 95 cases the average was 2.9 days. In 69 cases a fascial (modified Andrews) type of repair was used, with no known recurrence after two years. Among the cases where aponeurosis was not imbricated beneath the cord there were two recurrences.

The two recurrences in this series occurred, one at 16 months and the other at 18 months. Both of these herniae were originally indirect. Both recurrences were direct, coming through just lateral to the pubic tubercle. Both of them were reoperated upon by me. A Bassini type of repair had been performed in both instances. The transversalis fascia had not been plicated in the posterior wall of the canal. Dependence had been placed on the union of muscle to ligament. This line of union had stretched out to a thin layer of fibrous tissue with little resistance. There was no sign of muscle atrophy. There was no evidence of weakness in the region of the "muscle-split." Attention is called to the fact that both of these recurrences were among the early cases of the series when the "muscle-to-fascia" type of repair was employed and the medial part of the transversalis fascia was not tightened unless a direct hernia was present. In most of the subsequent operations this layer was plicated in the posterior wall of the canal and the internal ring was reconstructed. Only the fibrous portion of the conjoined tendon was utilized, dependence being placed on imbrication of the external oblique aponeurosis beneath the cord.

Sliding Hernia.—In the voluminous literature on hernia this type is rarely mentioned and recurrence statistics are even less frequently found. This may be due to the fact that the incidence of large sliding hernia is only about 2 to 5 per cent. There is little doubt, however, that in this group recurrence is relatively frequent.

Failure to cure sliding hernia may involve several factors. This type of hernia is not completely reducible and the contents of the sac are bulky. Therefore the defect in the abdominal wall is usually large, fascia split or thin and muscle displaced and atrophic. Proper reconstruction in such cases calls for a fascial transplant. If this is omitted recurrence may be expected in a majority of cases. The extensive dissection which precedes replacement of the prolapsed viscus may predispose to necrosis or infection. When the repair is completed the replaced viscus, usually cecum or iliac colon, lies just inside the weak spot ready to return to its former position at the first opportunity.

When a sliding hernia is encountered the intraperitoneal approach permits fixing the replaced bowel away from the hernial site without making another skin incision. Dissection may be done from above and below at the same time. When the parietal peritoneum has been sufficiently mobilized the viscus may be pulled upward so that when the peritoneum is closed it lies nearly two inches from the internal ring. Four large sliding herniae and one smaller one operated upon by this method have not recurred after two years.

Strangulated Hernia.—The intraperitoneal approach offers several advantages when dealing with a strangulated hernia. On opening the peritoneum above the internal ring one sees immediately what viscus is in the sac and proceeds accordingly. If it is safe to reduce the contents this can usually be done by gentle traction from the inside. Otherwise the peritoneum

may be slit from the original opening downward and the constricted internal ring cut under direct vision. The contents of the sac are inspected as they are replaced in the abdomen. If circulation is doubtful a tape may be passed around the bowel. This loop is reexamined after the repair and before the peritoneum beneath the muscle-split is closed. In the meantime the doubtful loop lies in its proper environment, protected from tension and chilling. Exposure is adequate for enterostomy or resection if indicated.

One patient in this series had a strangulated hernia the size of a large cantaloup. The internal ring was very small and tight. Within three minutes after the skin incision the contents of the sac (small bowel) had been replaced in the abdomen. This patient had no more postoperative reaction than the average elective case. Another patient was a man of 73 years, operated upon after this series was completed. His hernia had apparently been reduced the day before admission but pain and nausea persisted. A small mass could be felt beneath the muscles near the internal ring. At operation it was found that the contents (omentum) had been forced back out of the canal and lay in a dilated portion of the sac which was greatly indurated and adherent to the spermatic vessels and vas deferens as well as to the inferior epigastric vessels. This situation became relatively simple when the peritoneum was opened above the internal ring. Recovery of this patient was uneventful.

Incarcerated and Adherent Hernia.—When contents are adherent to a thin sac, back and within the internal ring, dissection may be tedious. All adhesions must be freed and no raw surface left after the sac is ligated. I have operated upon a number of recurrent herniae in which it seemed probable that such a raw surface adjacent to the internal ring was a factor in producing the recurrence. At times it may be difficult or impossible, from the classical approach, to mobilize the parietal peritoneum enough to permit removal of all damaged peritoneum when the sac is ligated.

When the intraperitoneal method is used this situation is under control. With the abdominal aspect of the internal ring in direct view adhesions are readily separated. If bowel is adherent within the sac, the sac may be opened at the internal ring above and through the canal below. Adhesions can then be freed by working alternately from either end. The neck of the sac is excised together with all doubtful peritoneum. The larger peritoneal defect thus produced can always be closed by mobilizing the parietal peritoneum.

Inguinal Hernia in Children.—It seems to be generally agreed that most herniae in children will be cured by high ligation of the sac alone. If this is true the less the cord is disturbed the better. A short incision may be made over the internal ring, the muscle split and peritoneum opened. The neck of the sac is excised. The sac itself may be split and left in place, if short. The sac can be easily separated from the cord and removed without disturbing the cremaster. This method leaves the cord undisturbed and makes certain high ligation of the sac. Six cases in this series were in chil-

dren. The average operating time was 12 minutes. There was very little postoperative reaction and none of the children needed opiates after operation.

There is another group of cases in which use of the intraperitoneal approach may be justified. It is becoming increasingly common for a man to request operation because he has been rejected for employment on account of hernia or apparent weakness in the inguinal region. Examination often shows nothing more than a slight impulse or an enlarged external ring. Again we may have a patient whose symptoms persist while the findings on examination are not conclusive. Often the man has been told that he will be given employment if his hernia is repaired. If we decide to operate upon one of these patients we are obligated not to weaken the inguinal region if no hernia is found. This can be done by the intraperitoneal method without disturbing the inguinal canal until it is evident that repair is indicated. The peritoneum can be opened above through a two inch skin incision. If a hernia is found the incision may be extended downward and the inguinal canal opened.

COMMENT.—The intraperitoneal approach, by adding a muscle-split to the usual incision, permits inspection or palpation of all inguinal hernia sites from within the abdomen. Its chief value lies in the fact that direct exposure of the internal ring is obtained without prolonging the operation or increasing the morbidity. The operation may be started in the usual manner. If the sac is not readily located or if the sac or its contents are unusually adherent the muscle may be split above the internal ring and the peritoneum opened in less than two minutes. The internal opening of the sac is found at once and its extent and contents noted. The adherent sac can be dissected more easily after its neck has been isolated and cut away from the parietal peritoneum. High ligation of the sac is made certain. In fact, the peritoneal neck of the sac and with it all raw surfaces which might lead to formation of adhesions is completely eliminated, leaving smooth peritoneum at the internal ring. Dissection around the neck of the sac is done under direct vision with the cord structures in full view. The internal ring may be reconstructed without damaging the cord or inferior epigastric vessels.

Easton,[12] commenting upon the operation advocated by La Roque, says: "Theoretically this operation seems to be subject to the disadvantage that it does not permit inspection of all possible hernial sites. It also has a tendency to weaken adjacent muscular structures and fails to strengthen the region of the internal opening of the hernia." I found no difficulty in any of the 100 cases in this series in inspecting the site of an indirect or direct hernia or in palpating the site of a femoral hernia. If a direct or femoral hernia is present I prefer to open the peritoneum through the posterior wall of the inguinal canal. In my cases there was no evidence that adjacent muscular structures had been weakened. I see no reason why this should happen if nerves are preserved and muscles are retracted gently. Concerning repair of the inguinal ring, I can say with certainty that the method used in this series gives excellent exposure of the internal ring and greatly facilitates its reconstruction.

This operation seems to be most useful in the unusual case, whether this be determined before operation, as in a strangulated hernia, or after the operation has begun and the ordinary approach found inadequate. If, on opening the sac, a sliding or unusually adherent hernia is found, time will be saved and a better result obtained by opening the peritoneum above. The operator should be able to visualize the anatomy of the inguinal region from the inner aspect, especially the transversalis fascia and position of the cord structures and inferior epigastric vessels at the internal ring. More than half the operations in this series were done by house surgeons under supervision.

CONCLUSIONS

The intraperitoneal approach for the repair of inguinal hernia, as described by La Roque, is a useful procedure with which the surgeon should be familiar.

It is suggested that this method be reserved for the unusual hernia or added to the classical operation when difficulty is encountered.

Direct exposure of the internal ring permits excision of the neck of the sac and accurate reconstruction of the ring itself.

The method has been found especially useful in operating upon strangulated or large sliding herniae.

The morbidity and recurrence rates were not increased in 100 cases operated upon by this approach.

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CORRELATION OF PATHOLOGIC AND ROENTGENOLOGIC FINDINGS IN TUBERCULOSIS AND PYOGENIC INFECTIONS OF THE VERTEBRAE

THE FATE OF THE INTERVERTEBRAL DISK

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ACCURATE interpretations of roentgenographic findings in diseases of the spine depend upon knowledge of the normal anatomy of the vertebrae and of the pathologic changes which may arise in them.

The studies of Schmorl[30] have helped to clarify our knowledge of the normal and pathologic anatomy. The difficulty in obtaining permission for the removal of the spine at necropsy and the infrequency of operative attack upon the vertebral bodies have resulted in a marked lack of reports of studies of vertebral pathology in the English literature. The fate of the radiolucent intervertebral disk in infections of the spine has been postulated upon the basis of clinical and roentgenologic observations.

Phemister[27] has shown that the contacted hyaline cartilages of joints of the extremities resist destruction from tuberculosis more effectively than from pyogenic infections. In our studies of the pathology of the spine we have found evidence that despite their differences in structure and function the intervertebral disk reacts to infections much as does the cartilage of the knee or the hip joint. An attempt has been made in this study to correlate the pathologic and roentgenologic findings in tuberculosis and pyogenic diseases of the spine.

Anatomic Considerations.—An individual vertebra is formed from three primary and five secondary centers of ossification. The primary centers, one each for the vertebral body and for each half of the neural arch, are present at birth. The secondary centers develop in the tip of each transverse process, the tip of the spinous process, and the marginal limit of each metaphysis of the vertebral bodies. These latter centers appear at puberty, may not fuse until the age of 25, and are referred to as the "epiphyseal ring." They are the rudiments of true epiphyses which completely cap the ends of the bodies of the vertebrae in lower animals, including the dog, rat, and cat.

Lexer and more recently Wagoner and Pendergrass[34] have studied the blood supply of the vertebral body and have shown that it is richly supplied with nutrient arteries which penetrate the cortex of the body into the spongiosa from all sides but do not cross the articular surfaces. The venous blood is collected into large sinusoids which, in turn, empty into the arachnorachidian veins, from which the flow is directed in the lumbar region into

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the inferior vena cava, in the thoracic into the azygos system, and in the cervical region into the main tributaries of the superior vena cava.

The structure of the normal intervertebral disk varies with the age of the individual. The fibrocartilaginous annulus blends intimately with the hyaline cartilage plates above and below and, with them, encloses the oval nucleus pulposus. The nucleus consists of an interlacing matrix of fibrous tissue and fibrocartilage, within the meshes of which is the semigelatinous nuclear substance which helps to maintain the form and contributes greatly to the resiliency of the normal disk. This material conforms to the law of fluids and

FIG. 1.—Tuberculous granulation tissue (t.b.) has extended between cartilage plate (c.p.) and bone, with gradual erosion of the cartilage. The nucleus pulposus (n.p.) and the annulus (a.f.) show no evidence of invasion.

is incompressible. Narrowing of the disk must be attended by dehydration, extrusion, or destruction of all or a part of the nucleus pulposus.

Blood vessels are not present in the adult intervertebral disk. Nutrition is supplied through the lymphatic system. Jung and Brunschwig[15] were able to demonstrate nerve fibers in the paravertebral ligaments, but none were found in the intervertebral disk.

Vertebral Tuberculosis.—Tuberculosis of a vertebra most commonly arises from a hematogenous implant in the spongiosa or compacta of the body, secondary to a lesion of lung or alimentary tract. The rare condition of vertebral infection by direct extension from tuberculous retroperitoneal lymph nodes has been reported by Fraser[10] and by Capener.[3] Harris[13]

reported tuberculous bacillemia and bacilluria in cases of bone and joint tuberculosis.

Judging from roentgenograms of early cases and from the available pathologic studies of early lesions, the infection nearly always begins within the body of the vertebra. Whether or not it is a primary metaphyseal lesion along the upper or lower limit of the body as in the diaphysis of a long bone or whether it begins in the spongy bone away from the articular ends is not definitely known. The case shown in Fig. 1 supports the metaphyseal theory. Kaufmann[16] believes that tuberculosis of a vertebra begins usually in the anterior portion of the body beneath the cartilage plate, but in some instances centrally, producing a diffuse caseous internal osteitis.

Keyes and Compere[17] showed that the adult disk is devoid of blood vessels and that nutrition must be maintained through osmosis and intercellular lymph spaces. No lymph vessels could be identified communicating from the vertebral body to the nucleus pulposus. Tuberculosis of the intervertebral disk would seem to be possible only by extension from foci in contiguous structures.

Thrap-Meyer,[32] after citing his own cases, and others from the literature, of multiple hematogenous infection in tuberculous spondylitis, stresses the infrequency of this occurrence.

Part I

Pathology of Vertebral Tuberculosis Uncomplicated by Secondary Pyogenic Infection

No case of primary tuberculosis of the vertebral appendages, the arch or the pedicles has been found in our series of cases, and we believe it to occur very rarely. Phemister and Hatcher[27] have reported their studies of tuberculosis of the extremity joints and have shown that tuberculosis granulations from an epiphyseal focus in adults may slowly erode the cartilage plate and penetrate into the joint. Figure 1 illustrates a similar process in the vertebra of an adult with slow erosion into the cartilage from a lesion in the metaphysis of the body. Such a lesion may be too small to be recognized in the roentgenogram until after prolapse of the nucleus pulposus and destruction of the disk, although the primary focus is definitely osseous.

The following cases, together with the necropsy findings, illustrate the clinical and pathologic nature of vertebral tuberculosis in children.

Case 1.—R. C., male, age 14, was admitted to the University of Chicago Clinics December 9, 1931, with a diagnosis of tuberculosis of the spine and right hip. The initial focus had been in the vertebral column and was first noted in October, 1923. Arthrodesis of the spine was performed in November, 1924, with clinical evidence of healing.

Tuberculosis of the right hip had been diagnosed in 1929 and abscesses had developed over the greater trochanter. The hip was successfully fused September 25,

1931. In July, 1932, the patient developed signs of meningeal irritation and died August 5, 1932, at the age of 15, of tuberculous meningitis. At necropsy a segment of the spine from thoracic 5 to lumbar 1 inclusive was removed.

Pathology.—The gross sagittal section of the spine (Fig. 2a) includes the vertebrae from T 5 to L 1. From T 6 to T 12, the arches are fused into a solid bony plate. The fragments of the vertebral bodies of T 8 and T 9 have fused together. The centrum of T 7 shows a slight loss of contour.

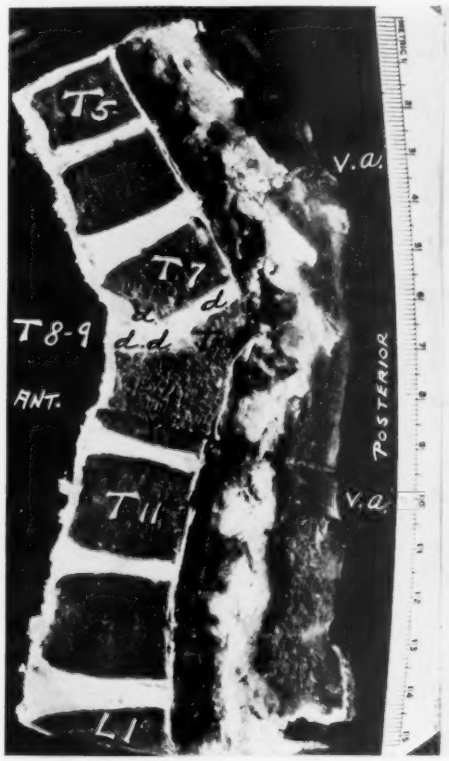

FIG. 2a.—(Case 1) Age 15. Tuberculosis, healed. Photograph of split spine section from T 5 to L 1. At the apex of the kyphos are two small wedge-shaped bony masses, remnants of the bodies of T 8 and T 9. Portions of disk T 7–8 (d) and disk T 9–10 (d.d.) may yet be identified. The vertebral arches (v.a.) show surgical fusion from T 6 to T 12.

FIG. 2b.—Roentgenogram of gross specimen. Bony fusion (b.f.) between T 7 and the collapsed mass of T 8 and T 9 is almost complete and partial fusion (b.f.) is present across the intervertebral space of T 9 and 10. The posterior two-thirds of this disk (d.d.) is persistent but narrowed. No evidence of active tuberculosis is seen in either illustration. *Note.*—This is a healed case of tuberculosis of the spine and does not show the sclerosis, sequestration or other presumptive evidence of pyogenic infection which was recently described by Finder in a case of vertebral tuberculosis with multiple abscesses and discharging sinuses. This case and Cases 7, 8 and 9 indicate that changes, which Finder thought to be brought about by the healing process in vertebral tuberculosis, obtain only when there is a dual infection.

The disk between the wedged vertebrae and the centrum below has been completely disrupted in its posterior portion and anteriorly represents the remnants of disk T 8–9 and T 9–10. Disk T 7–8, at the cephalic margin, appears well preserved. In this gross specimen there is no recognizable area of disease.

The roentgenogram of the split spine section (Fig. 2b) shows the fused and wedged

FIG. 3a.—(Case 1) Age 15. Tuberculosis. Centra T 7 to T 10 with intervertebral disks are included. The high degree of wedging of the bodies of T 8 and T 9 (v.b.) is well illustrated. Disk T 6–7 (iv.d.) is grossly intact eight years after spinal fusion. A part of the annulus (a.f.) and nucleus pulposus (n.p.) of disk T 7–8 has survived the infection (×2).

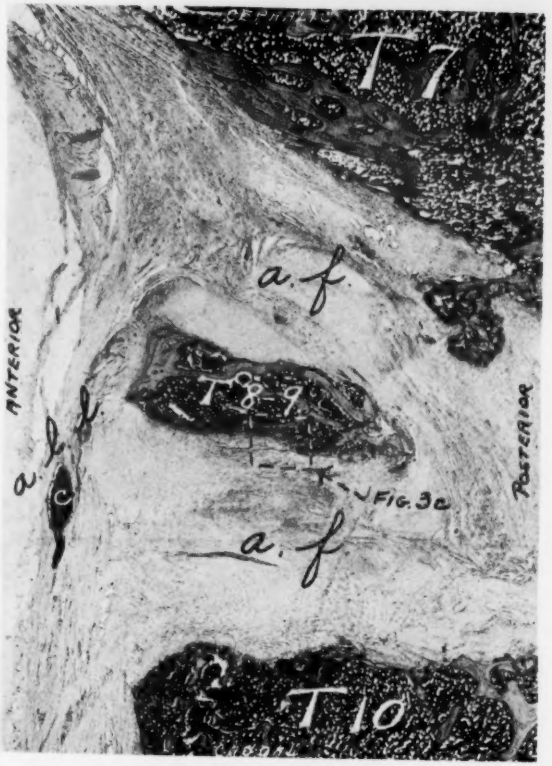

FIG. 3b.—A higher magnification showing the remnants of the anterior portion of T 8 and 9, with the fibrous element of the adjacent disks (a.f.). A small area of calcification (c) is present in the anterior longitudinal ligament (a.l.l.). Osseous invasion of disk substance may be noted at (b.) (×10).

FIG. 3c.—Section through the distomedial portion of T 8 and T 9, with the surrounding disk substance. There is some preservation of the cartilaginous (c.p.) and fibrous tissue (a.f.) of the disk even after extensive destruction of this part of the spine. There is no microscopic evidence of active tuberculosis (×210).

remnants of the bodies of T 8 and T 9. Partial osseous fusion exists between these crushed centra and the vertebrae above and below. Both proximally and distally, however, portions of the intervertebral disk space of T 7–8 and T 9–10 may be identified. All other vertebrae and disks present an essentially normal appearance. The laminae appear to be fused. There is no roentgenographic evidence of active tuberculosis.

The vertebral bodies of T 7 to T 10 are included in the microscopic section (Figs. 3a, b, and c). Normal hematopoietic marrow is present throughout, even in the

FIG. 4a.—(Case 2) Age 6. Tuberculosis. Photograph of split section from T 7 to L 2, with portions of T 6 and L 3. The centra from T 9 to L 1 have collapsed to form a caseous mass, in which small remnants of the disks (d.) are still visible. Beginning anterior erosion of disk L 1–2 is seen at (a). while similar invasion (B.c.) is occurring into the bodies of T 7 and 8. Caseous debris is present in the spinal canal at the level of T 9 and T 12 (s.).

FIG. 4b.—This roentgenogram of the split section shows necrosis and collapse of the centra from T 9 to L 1. Parts of three intervertebral spaces (d.) persist. Note anterior erosion (a.b.) of the bodies of T 7 and T 8 and backward protrusion of partially calcified material into the spinal canal (c).

crushed remnant of T 8 and 9. There is no inflammatory process or fibrous tissue reaction within the bodies. The intervertebral disk T 6–7 appears to be normal. The disks between T 7 and 8 and T 9 and 10 exist as irregular fibrous bands with a few areas of cartilage. Disk T 8–9 has been completely disrupted. The nucleus pulposus material of disk T 7–8 has been reduced in quantity, either by dehydration or loss into

the spongiosa or ligaments. The hyaline cartilage plates of the posterior fourth of the disk of T 7–8 are still intact, while those of disk 9–10 have almost completely disappeared. A small calcified area is present within the substance of the anterior ligament slightly below the level of the collapsed centra. No area of active tuberculous tissue could be found in the sections.

COMMENT.—This represents a case of healed tuberculous spondylitis of nine years' duration, in which meningitic infection occurred, probably not from the spine but from a hematogenous implant within the spinal canal.

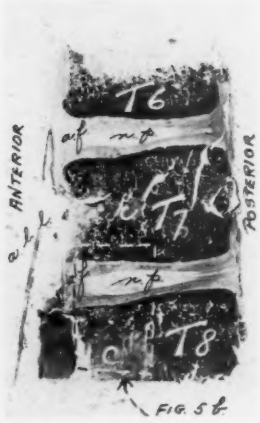

FIG. 5a.—(Case 2) Age 6. Tuberculosis. The centrum of T 7, with a portion of T 6 and T 8. The annulus (a.f.) and nuclear structure (n.p.) of the disks are well preserved. Caseous débris has spread beneath the anterior ligament (a.l.l.) with invasion of T 7 and T 8 (c.) (×2).

FIG. 5b.—A portion of disk T 7–8 and the adjacent vertebral bodies. The annulus fibrosus (a.f.) and nuclear structure (n.p.) of the disk are intact. The areas of caseation (t.c.) in the centra extend to, but do not cross, the plates of hyaline cartilage (c.p.). There are many tubercles, most of which are undergoing central caseous necrosis (×13).

The tuberculosis of the hip was found to be quiescent but not healed and this may have been the source of the meningeal infection. There is collapse of two of the centra, with crowding together of the arches. Osseous destruction is more marked than is that of the fibrous and cartilaginous portions of the intervertebral disks.

Case 2.—E. H., male, age 6, was admitted to the University of Chicago Clinics February 26, 1932. The onset of symptoms was six months previous to admission. At the age of five and one-half years a definite kyphos was noted in the lower thoracic spine associated with night cries and daily elevation of temperature. The patient also had a left otitis media, which was probably tuberculous.

The course was continually downhill in spite of complete bed rest, immobilization,

and supportive treatment. No operation was performed. Tuberculous meningitis was diagnosed in June, 1932, and the patient died June 24, 1932, at the age of six years, nine months. A segment of the spine from T 6 to L 3 was removed at necropsy.

Pathology.—The split section (Fig. 4a) includes eight vertebrae from T 6 to L 3. The infection has spread by extension both upward and downward beneath the anterior ligament which is raised from the centra over the infected bodies by caseous material. Five vertebrae (T 9 to L 1) are almost completely replaced by caseous necrosis and their partial collapse anteriorly has produced mild kyphosis. Caseous material has extended into the spinal canal at L 1 and also above the level of the kyphosis. The anterior portions of the intervertebral disks show invasion by direct extension of the infection from the tuberculous abscess.

A roentgenogram of the section (Fig. 4b) shows partial destruction or collapse of the centra from T 9 to L 1, with indefinite preservation of the intervertebral spaces. The disk space between T 12 and L 1 has been completely lost and the bodies are united in a caseous and calcareous mass which is encroaching upon the spinal canal. Roentgenographic evidence of anterior invasion is seen in the centra of T 7 and T 8.

A satisfactory microscopic section through the most necrotic vertebrae could not be made. The microscopic studies include sections of the bodies of T 6, 7 and 8, with their intervening disks (Figs. 5a and b). At the level of disk T 6–7 the anterior ligament is firmly attached to the annulus, marking the upper limit of spread of the infection.

Many tubercles may be seen in the cancellous bone of T 7 and T 8 showing circumferential spread and destruction of trabeculae. The anterior part of the centrum of T 8 exhibits involvement from the abscess beneath the paravertebral ligament in a wedge-shaped area of necrosis separated from the living osseous tissue by a wall of granulations. The centrum of T 7 has been similarly invaded.

The cartilage plates and the intervertebral disks appear to be grossly normal. At the posterodistal margin of disk T 7–8 a microscopic fissure may be seen in the cartilage plate with beginning invasion of fibroblasts and leukocytes.

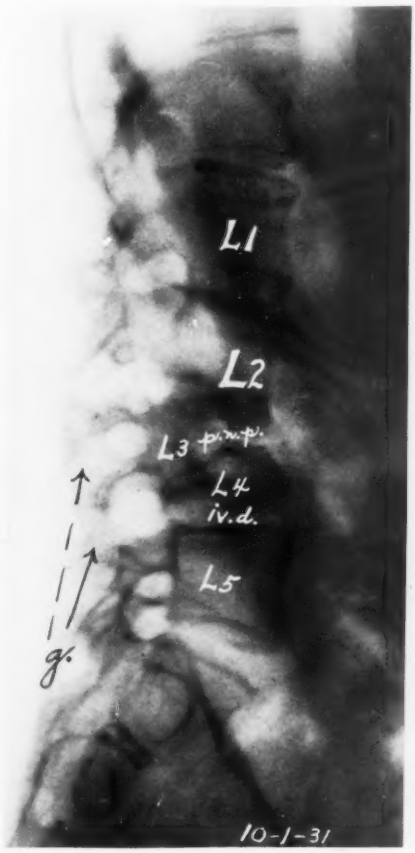

FIG. 6.—(Case 3) Age 13. Tuberculosis. Roentgenogram taken October 1, 1931, a month before the second spinal fusion and two months, three days antemortem. The bodies of L 2, 3 and 4 are wedged and have undergone partial osseous fusion, but with some preservation of the intervertebral space between the anterior edges of L 2 and L 4. The nucleus pulposus (p.n.p.) of disk L 2–3 has prolapsed into the centrum of L 2. Disk space L 4–5 (iv.d.) appears uninvaded. A portion of the graft (g.) may be identified.

COMMENT.—This case demonstrates the spread of vertebral tuberculosis by extension beneath the anterior paravertebral ligament, with involvement of the centra and to a lesser degree destruction of the intervening disks by anterior invasion.

Case 3.—C. C., female, age 13, was admitted to the University of Chicago Clinics February 24, 1931, because of tuberculosis of the second, third, and fourth lumbar vertebrae first diagnosed at the age of six years.

Treatment had consisted of intermittent periods of immobilization in a plaster encasement or on a Bradford frame. An Albee type of fusion was performed March 2, 1931. At operation the spines and laminae of the lumbar segments were found to be extensively eroded and replaced by tuberculous caseation. The bone graft was attacked by the infection and a fracture then occurred at the site of maximum splinting stress. A second spinal fusion operation was performed November 11, 1931 (Fig. 6), but the patient died of tuberculous meningitis December 4, 1931. A segment of the spine from T 11 to L 5 was removed at necropsy.

FIG. 7a.—(Case 3) Age 13. Tuberculosis. Shows the centra of L 2 and 4 and a part of L 5. The small remnant of L 3 is not included in the section. Three small centers of ossification (e.) representing the epiphyseal ring are seen in disk L 4–5 (iv.d.) (×2).

FIG. 7b.—Includes L 4 with the adjacent disks and a small portion of L 2. The persistent annulus (a.f.) and the prolapsed nucleus pulposus (p.n.p.) of disk L 2–3 are noted (×10).

Pathology.—Vertebral bodies L 2, 3 and 4 are compressed both in the anteroposterior and lateral diameters. Disk L 3–4 has been destroyed and there is fibrous union between the two centra. Disk L 2–3 is still present anteriorly but partial destruction has occurred in its posterior portion. Disks L 1–2 and L 4–5 appear to be intact.

The microscopic section includes a portion of L 2 and 5 and all that remains of the bodies of L 3 and 4 (Fig. 7a and b). Tuberculous granulation tissue can be identified in the anterior paravertebral ligament in contact with the centra of all of these vertebrae. Disk L 2–3 has been broken through, with herniation of the nucleus pulposus into the spongiosa.

COMMENT.—This represents a case of vertebral tuberculosis with destruction of two adjacent centra and preservation of a portion of the corresponding disk elements. Although the pedicles, laminae and spinous processes of the diseased vertebrae show caseous tuberculous necrosis, greater destruction of the centra leads us to postulate that the appendicular involvement was secondary to that in the bodies. Erosion of the inferior cartilage plate of L 2 was followed by extrusion of a portion of the nucleus pulposus into the necrotic tuberculous spongiosa.

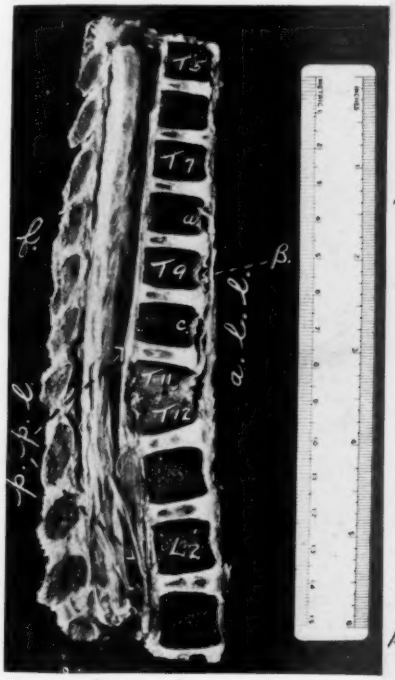

FIG. 8a.—(Case 4) Age 2. Tuberculosis. Photograph of split section from T 5 to L 3. The bodies of T 11 and T 12 are wedged, with disruption of the disk and loss or extrusion of the nucleus pulposus. Abscess or débris has migrated beneath the anterior ligament with invasion of three centra (a.b.c.). The posterior ligament (p.p.l.) is elevated over T 11 and T 12.

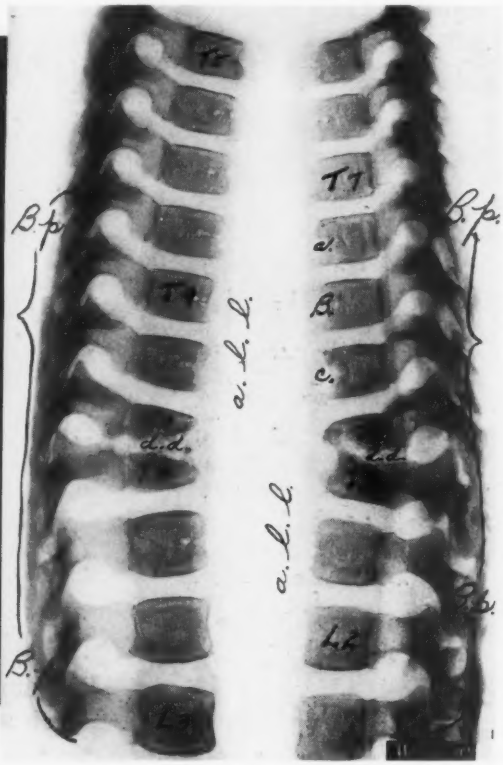

FIG. 8b.—Roentgenogram of section shown in Fig. 8a. The collapse and wedging of T 11 and T 12 are shown, with the irregular narrowing of the intervertebral space (d.d.). There has been anterior invasion of the centra of T 8, 9 and 10 (a.b.c.). From T 7 to L 3, the lamina are fused into a solid bony plate (b.p.).

Case 4.—J. L. M., female, age 16 months, was admitted to the University of Chicago Clinics May 24, 1934. She had been treated for one year for acute bilateral miliary pulmonary tuberculosis. There was a history of direct contagion from the mother who had an active pulmonary lesion. An abscess shadow was noted about the lower thoracic spine in the chest roentgenogram of May, 1934. Lateral roentgenograms of the spine showed a definite destructive lesion in the eleventh and twelfth thoracic vertebrae. A review of earlier roentgenograms showed that this abscess shadow, although not previously discovered, had been present and enlarging for at least six months.

A spinal fusion operation was performed June 4, 1934. The patient made an uneventful postoperative recovery, but two months later developed signs of meningeal irritation and subsequently died of tuberculous meningitis October 12, 1934, at the age of two years and ten months. A section of the spine from the fifth thoracic to the third lumbar vertebrae was removed at necropsy (Fig. 8a).

Pathology.—There is no gross evidence of direct extension of tuberculosis from the diseased spine or abscess through the dura and into the spinal canal. The spine is adequately splinted by the fusion operation.

Contiguous portions of the centra of T 11 and 12 are collapsed and somewhat wedged. The intervening disk has been almost completely destroyed and the intervertebral disk space is represented by a single abscess cavity, about the margins of which remnants of the annulus fibrosus and cartilage plate can still be identified. Posteriorly, this abscess presses upon the dura, and the posterior ligament has been raised from the diseased centra by the migration of pus and débris beneath it (Fig. 8a).

The anterior paravertebral ligament has been elevated from the vertebral margins from disk T 7–8 to disk T 12 by upward extension of the abscess. Definite invasion of the anterior margins of the centra of T 8, 9 and 10 can be seen, but the corresponding intervertebral disks are intact.

The roentgenogram of the split spine section (Fig. 8b) shows wedging and triangularization of the shadows of the bodies of T 11 and T 12, with disruption of the intervening disk space. The areas of anterior invasion of T 8, 9 and 10 noted in the split spine sections are shown in the roentgenogram. The laminae from T 8 to L 3 are fused into a strong plate of bone.

The microscopic sections include the centra from T 8 to L 1, with their intervening disks (Figs. 9a, b and c). A few fragments of hyaline cartilage plate and portions of the annulus fibrosus may be identified in the borders of the cavity between T 11 and T 12. The anterior ligament has been raised from the vertebral margins by tuberculous exudate and granulation tissue containing tubercles lines the abscess cavity.

The trabeculae of T 11 and 12 are atrophic about the margins of the old disk area and the normal marrow has been replaced by diffuse fibrous tissue. The anterior invasion into the centra of T 8, 9 and 10 is by direct extension from the tuberculous abscess. Complete preservation of the intervening disks is again noted.

Comment.—This constitutes a study of a case of acute vertebral tuberculosis. Extension of an abscess into the spinal canal without perforation of the dura has been demonstrated. The meningeal infection was diffuse and generalized and probably occurred from hematogenous extension, or by direct spread of organisms through the dura by the lymphatics at level T 11 and 12. The anterior invasion of three vertebral bodies, with complete preservation of the intervening disks shows the usual method of spread of the disease in the spine and again demonstrates the tendency of tuberculosis to invade and necrose cancellous bone more readily than mature fibrous tissue or cartilage.

Discussion: Part I.—This pathologic study of four cases of tuberculosis of the spine indicates that the finding that cartilage is less readily destroyed by tuberculous exudate, than is bone, is as true of the fibrous and cartilaginous portions of the intervertebral disk as it is of the hyaline cartilage of the knee or hip joints. Remnants of intervertebral disk substance may persist after the contiguous vertebral bodies have been disrupted by the tuberculous infection.

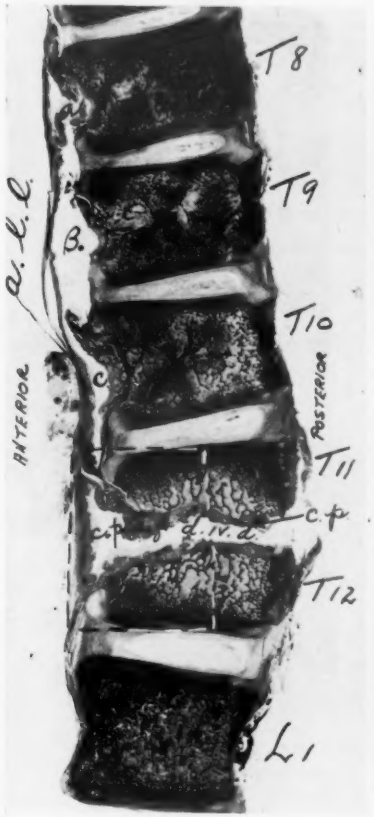

FIG. 9a.—(Case 4) Age 2. Tuberculosis. The infection has been most active in the bodies of T 11 and T 12, with destruction of a large part of the intervening disk (d. iv. d.). A tuberculous abscess has extended beneath the anterior ligament and invaded the anterior portions of the centra of T 8, 9 and 10 (a.b.c.) (×2).

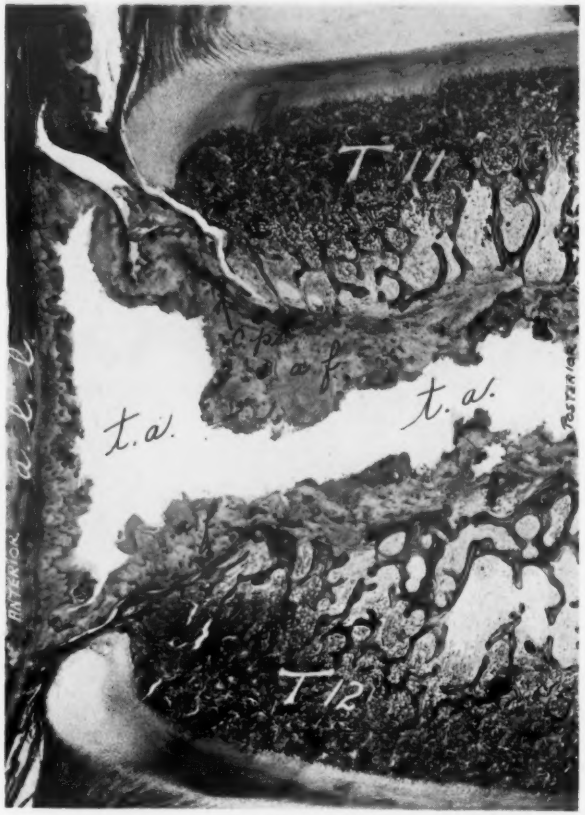

FIG. 9b.—Section through the anterior portion of disk T 11–12 which has been replaced by a tuberculous abscess (t.a.) in the walls of which are many tubercles. The contiguous portion of each adjacent centrum has been invaded and destroyed by the disease. A portion of the annulus (a.f.) persists and a few small remnants of the cartilage plates are noted (a.p.) (×10).

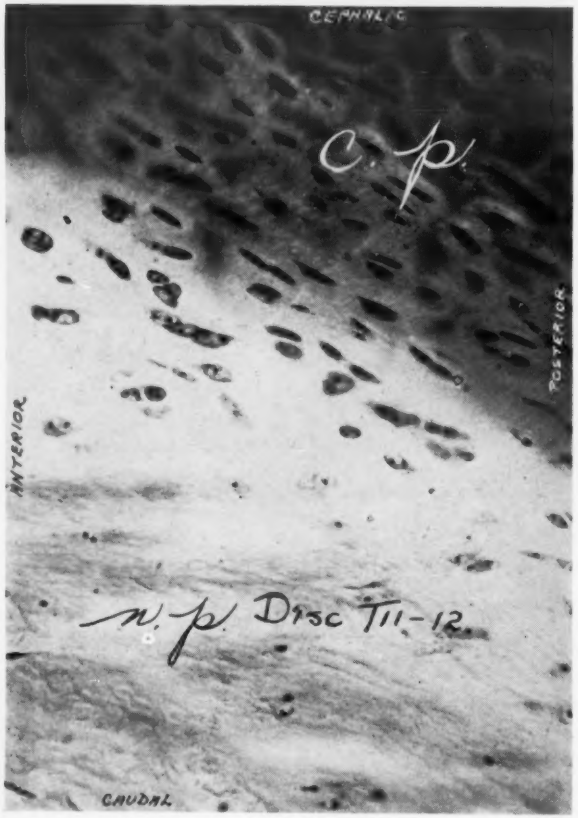

FIG. 9c.—Section through a remnant of disk T 11-12, showing preservation of a portion of the nucleus pulposus (n.p.) and cartilage plate (c.p.) (×210).

Spread of tuberculosis from centrum to centrum through the intervertebral disks has not been noted in our studies. These patients were young children or adolescents and the cartilage plate, a continuation of the epiphyseal rim cartilage, is thicker during the growth years, constituting a more effective barrier to the direct spread of the disease than obtains in the adult spine. Instead, the tuberculous exudate had spread by extension beneath the paravertebral ligament about the periphery of the intervertebral disk from body to body in three cases in which the disease was still active, and posteriorly into the spinal canal in two cases. No area of direct extension through the dura and direct involvement of the spinal cord was noted.

Tubercles in the spongiosa, when present, are of characteristic appearance, with round and epithelioid cells around central necrotic foci, many of which contain giant cells. In some sections, although spongiosa and cortex were converted into tuberculous débris, with necrosis, collapse and partial absorption of the bone, no typical tubercles could be found.

As has been shown in previous communications,[12, 30] any damage to the cartilage plate, the result of trauma or disease, may permit escape of all or a part of the nucleus pulposus, with reduction in size and loss of contour of the intervertebral disk. This loss of the semifluid nuclear material may explain the narrowing of the disk line occasionally seen in the early roentgenogram in tuberculosis of the spine. Because of the incompressibility of the nucleus pulposus, any change in the shape of the disk must be attended by change in or escape of this nuclear material.

Primary tuberculous invasion of the annulous fibrosus has not been demonstrated but erosion of the disk structure by caseous débris beneath the anterior paravertebral ligament is not uncommon.

In vertebral tuberculosis without secondary pyogenic infection, there is little tendency toward regeneration of bone. Albee[1] and Delchef[6] have argued that this lack of new bone formation justifies the utilization of the tibial bone graft for a firm spinal arthrodesis.

The neurologic aspect of vertebral tuberculosis includes the formation of epidural or subdural abscesses, with direct or hematogenous spread to the tissues of the central nervous system. The spinal cord may be crushed by collapse of the centra but this is an uncommon occurrence and has not been found in our cases.

The symptom-syndrome described as "Pott's paralegia" may be due to pressure on the cord by posteriorly displaced disk substance, necrotic tuberculous débris or extradural abscess within the spinal canal or to edema of the cord occurring secondary to the regional inflammation.

Tuberculous peritonitis is a rare sequela of vertebral disease, while meningitis is relatively common. Acute miliary tuberculosis has followed the spinal infection. Dissemination of the infection may be from the diseased vertebrae or by invasion of the blood stream (Corret, Michon, and Reny[5]), from the original focus in the lung or lymph nodes. Fossel[11] has described a

case of generalized miliary tuberculosis following the erosion of spinal caries into the aorta.

Part II

VERTEBRAL OSTEOMYELITIS

In pyogenic infections of the spine as in vertebral tuberculosis, the primary focus is in the bone and not in the joints. The intervertebral disk is less able

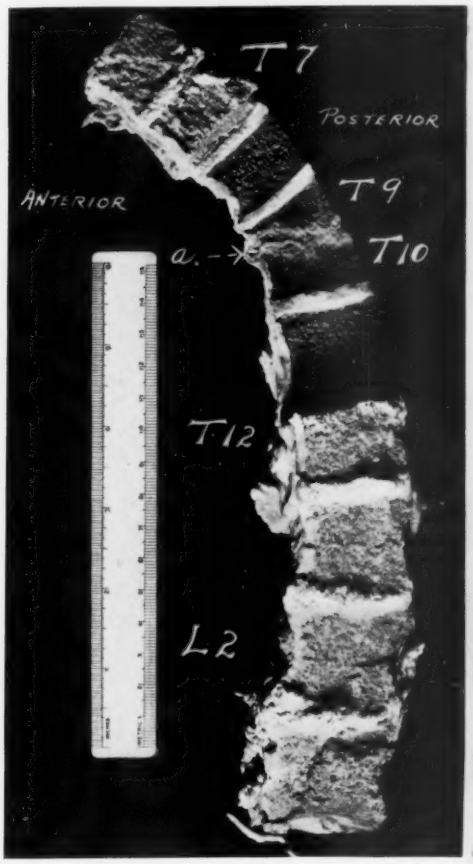

Fig. 10a.—(Case 5) Age 55. Osteomyelitis. Photograph of split section from T 6 to L 3. The bodies of T 10 and especially T 9 are partially collapsed anteriorly. Disk T 9–10 has been disrupted and a portion of it extruded anteriorly (a.). Other bodies and intervertebral disks are intact.

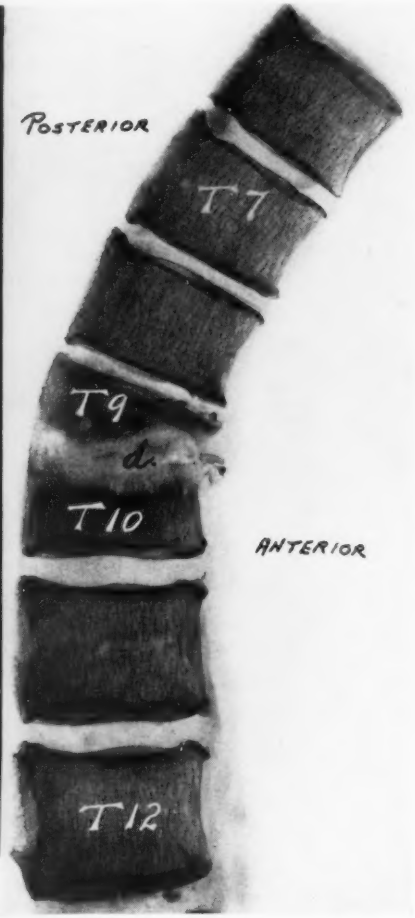

Fig. 10b.—Roentgenogram of split spine section. Irregular absorption of the contiguous halves of T 8 and T 9 produces the wedging described in Fig. 10a. The disk area (d.) has lost its contour and the tissue filling the disk space casts a mottled shadow suggesting beginning ossification.

to survive the attack of pyogenic disease and the following cases showed early roentgenographic evidence of loss of intervertebral space.

Case 5.—F. C. T., male, age 55, was admitted to the University of Chicago Clinics October 4, 1933. The patient gave a history of pain in the lower thoracic spine of eight

FIG. 11a.—(Case 5) Age 55. Osteomyelitis. Disk T 9–10 has been completely disrupted (d.d.). The necrotic remnants of this disk and a portion of the nucleus pulposus (p.m.p.) have been extruded anteriorly beneath the paravertebral ligament (a.l.l.). New fibrous tissue (f.t.) bridges the posterior portion of the old disk space (×2).

FIG. 11b.—A higher magnification through the extruded disk débris (p.n.p.) and the intervertebral space (d.d.) of T 9 and T 10. The anterior ligament (a.l.l.) about the extruded disk substance is covered on its inner surface by a pyogenic membrane (p.m.). A small portion of the annulus (a.f.) is present at the osseous margins. The bone trabeculae have been extensively destroyed by direct extension of the infection (×10).

FIG. 11c.—Fibrous tissue (d.f.) extends across the old disk space of T 9–10. New bone trabeculae are present at the disk margins but do not extend across (n.b.). Some devitalized hyaline cartilage (d.c.) may be seen posteriorly at the upper edge of the former disk space (×10).

weeks' duration. Two weeks before the onset of symptoms, he had been confined to bed with an illness thought to be influenza. Abdominal pain developed and this later localized in the lower dorsal spine.

The lateral roentgenogram showed gross destruction of the intervertebral disk T 9–10 and of the approximating portions of the centra. The condition was diagnosed tuberculosis and a spinal fusion was performed October 23, 1933. The patient had a severe postoperative reaction and died the following day. Necropsy revealed multiple septic foci, including pyelonephritis, infarcts of the spleen and kidneys, and acute generalized peritonitis. A sagittal section of the vertebral bodies from T 6 to L 3 was removed.

FIG. 12a.—(Case 6) Age 17. Osteomyelitis. The bodies of T 11 and T 12 are joined by new bone trabeculae. Disk T 11–12 is represented by two small cartilaginous inclusions (c.c.), and a posteriorly situated abscess cavity (a.c.) is the only remaining focus of the pyogenic infection. The defects in the cartilage plates of the disk below are precursors of nucleus pulposus herniations, as described by Schmorl (d.c.p.) (×2).

FIG. 12b.—Section through the area of disk T 11–12, showing the cartilage inclusions (c.c.), and the complete osseous union of the two vertebrae (n.b.) (×10).

Pathology.—Vertebral bodies T 9 and 10 are eroded on their contiguous surfaces. The disk between these two vertebrae has been destroyed and replaced by fibrous tissue and exudate which bulges anteriorly into the paravertebral ligament. No gross abscesses or sequestra can be identified.

The roentgenogram of the sectioned spine (Fig. 10b) shows wedging of T 9, partial loss of contour of T 10 and destruction of the disk, with anterior protrusion of a portion of its substance. Adjacent vertebrae are grossly and roentgenologically normal.

Four vertebrae are included in the microscopic sections (Fig. 11). Disk T 9–10 has been almost completely destroyed. Small islands of articular cartilage are present at each end of the old disk space. The posterior half of the annulus has been replaced by granulation tissue containing areas of new bone formation. The anterior half is largely necrotic and contains small collections of fibrin and polymorphonuclear leukocytes. There are small islands of newly formed bone in the cancellous bone bordering the interspace.

COMMENT.—The nature of the onset, short duration, severity of the symptoms, rapid destruction of the disk substance, and the acute bone necrosis shown in the roentgenogram should have established the correct diagnosis of pyogenic osteomyelitis.

Pathologic studies indicate that extension was through the disk with disruption of its structure, but the primary focus of infection could not be definitely established. Greater destruction of T 8 than T 9 might indicate that the former was primarily involved. There was no migrating paravertebral abscess.

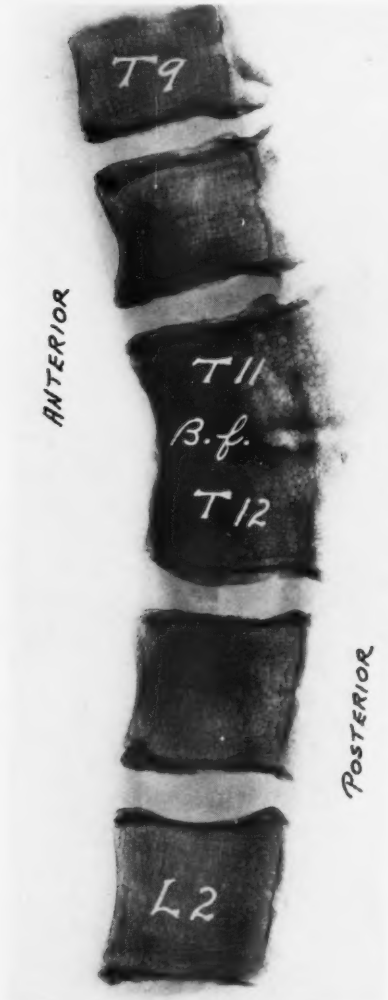

FIG. 13.—(Case 6) Age 17. Osteomyelitis. Roentgenogram of split section of vertebral bodies. There has been only a small loss of substance of the bodies of T 11 and T 12, but complete loss of the intervertebral space. Bony fusion (b.f.) is present between these two vertebrae. The other disks and vertebral bodies are intact.

Case 6.—C. H., male, age 14, was admitted to the University of Chicago Clinics November 20, 1931, with a diagnosis of pyogenic arthritis of the right hip and multiple osteomyelitis.

The onset was acute, but there were no symptoms referable to the spine until three years later when a minimal deformity in the lower dorsal spine was noted. A large retroperitoneal abscess was diagnosed and drained July 17, 1934. A roentgenogram on July 19, 1934, showed partial destruction of the centra of T 11 and T 12, with complete obliteration of the disk space.

Death occurred August 7, 1934, from generalized amyloidosis. A section of the spine removed at autopsy included vertebrae T 9 to L 2.

Pathology.—The split spine section shows the complete disruption of the intervertebral disk between T 11 and 12 with osseous union of the two centra. The microscopic section of disk T 12–L 1 shows a small break in either cortex with beginning extension of the adjacent fibrocartilaginous tissue into the vertebral bodies (Fig. 12).

Two cartilage islands, surrounded by bone, are still present at the site of disk T 11–12, and posteriorly at this level there is a small abscess. The bone of the fused region and for a great distance away contains marrow made up of granulations and fibrous tissue.

The roentgenogram of the section (Fig. 13) shows the osseous fusion between the centra of T 11 and T 12, with loss of intervening disk space, and moderate wedging of the shadows of these vertebrae anteriorly, producing mild kyphosis.

COMMENT.—This case illustrates destruction and osseous replacement of intervertebral disks in pyogenic spondylitis. New bone formation, common in the healing of pyogenic osteomyelitis, is shown.

DISCUSSION: PART II.—Pyogenic vertebral osteomyelitis is commonly a hematogenous infection, secondary to a focus of infection elsewhere in the body. According to Volkmann,[33] the initial focus of pyogenic vertebral osteomyelitis is in the neural arch more frequently than in the vertebral body. In his series of 70 cases of pyogenic infections of the spine, 59 per cent showed involvement of the arch or its processes, 34 per cent involvement of the body, while in the remaining 7 per cent both were affected. This analysis was based partly on autopsy and partly on clinical and roentgenologic studies of his own cases and those reported by others. Kulowski[19, 20] has recently reported an excellent clinical study of pyogenic osteomyelitis of the spine. His statement that some of his patients showed primary hematogenous intervertebral disk infections cannot be reconciled with the anatomic fact that this structure is avascular.

In contrast to tuberculous spondylitis, there is a rapid and early involvement of the intervertebral disk in pyogenic infection of the vertebrae. The cartilage plate is rapidly destroyed by the proteolytic enzymes formed in pyogenic exudate and the nuclear substance is extruded. The fibrous annulus also undergoes dissolution. This is comparable to the destruction of articular cartilage of joints of the extremities as it is known to occur in severe pyogenic arthritis.

When the acute infection subsides there is regeneration of bone, and ankylosis of vertebral bodies occurs much more commonly and more rapidly than in cases of tuberculosis of the spine. Persisting sequestra are uncommon, as spongy dead bone is quickly absorbed, but when present may be found within the spongiosa of the vertebral body or in the compacta of the arch. Volkmann reports more frequent sequestration of the spinous process when this part of the arch is involved.

PART III

VERTEBRAL TUBERCULOSIS COMPLICATED BY PYOGENIC INFECTION

Secondary pyogenic infection is a frequent complication of tuberculosis of the skeleton when a cold abscess is incised or opens spontaneously to the surfaces of the body. This combination of pyogenic and tuberculous infection decreases the patient's chances of recovery. Sinuses of this type characteristically do not heal, and generalized amyloid disease and death may result from the infection and the continued loss of body proteins in the exudate. The pathologic changes that occur in the spine from this mixed infection may be typical of either tuberculosis or of pyogenic osteomyelitis, or a combination of the two.

Case 7.—F. E., male, age 17, was admitted to the University of Chicago Clinics July 8, 1931. A diagnosis of tuberculosis of the thoracolumbar spine had been made in 1923. Drainage from a lumbar abscess had been present since 1926.

A spinal fusion was performed July 20, 1931. The immediate postoperative course was satisfactory and there was clinical improvement for a period of almost two years. The sinuses did not heal, although postoperative roentgenographic studies indicated osseous re-

pair in the spine. Amyloid disease was present, renal insufficiency became more marked and death occurred April 16, 1934, at the age of 19 years, 10 months.

The diseased section of the thoracolumbar spine was removed at autopsy.

Pathology.—The split spine section shows a marked dorsolumbar kyphos with complete destruction of the bodies of T 10 to L 1 with the exception of the posterior part of T 10 (Fig. 14a). The bodies of L 2 and L 3 show partial osseous union with loss of disk substance. The presence of necrotic material, surrounded by fibrous tissue, beneath the interior ligament at the level of the kyphos indicates the mode of spread of the infection. The intervertebral space at the apex of the kyphos is occupied by a small abscess posteriorly

FIG. 14a.—(Case 7) Age 19. Tuberculosis and Secondary Pyogenic Infection. Photograph of split section of lower thoracic and lumbar spine. The bodies of T 10 to L 1 are destroyed. At the level of the kyphos (k.), a portion of the tenth thoracic body (b.) projects into the spinal canal. Bony fusion (b.f.) has occurred between the bodies of L 2 and L 3. The disk (d.) is preserved in its anterior half, while lower thoracic disks are completely disrupted. Necrotic débris (n.) is present beneath the anterior ligament.

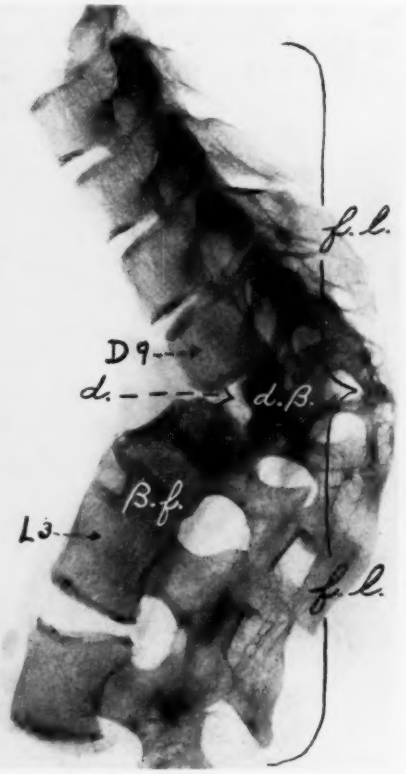

FIG. 14b.—Roentgenogram of the previous section. Four centra (d.b.) at the thoracolumbar junction have been largely destroyed, leaving an irregular intervening space (d.). The second and third lumbar vertebrae show intimate bony fusion (b.f.). The surgical union of the laminae (f.l.) splints the diseased segment of the spine.

and by fibrous tissue anteriorly. Immediately in front of it there is another abscess pocket surrounded by thick fibrous tissue. The notch anteriorly between the partly fused bodies of L 2 and 3 is filled by fibrous tissue. The arches posteriorly are joined by a strong plate of bone in which the tibial bone grafts are firmly united to, and blended with, the laminae. The meninges and cord are free.

A roentgenographic study of the section (Fig. 14b) shows the extensive destruction of the bodies of the three lower thoracic and the first lumbar vertebrae, with bony fusion

of L 2 and L 3. There is osseous fusion of the laminae from the eighth thoracic to the third lumbar.

The microscopic section includes portions of seven vertebrae (Fig. 15). Four bodies and intervertebral disks have been destroyed by the infection. The disk between D 9 and D 10 is represented by three isolated cartilage islands and a remnant of fibrous tissue.

At the level of the kyphos the three abscess cavities are lined with a pyogenic membrane and filled with necrotic débris and the walls are heavily infiltrated with lymphocytes (Fig. 15a and b). Islands of epithelioid cells are also present. The marrow of the vertebrae bordering this region has been in part replaced by fibrous tissue, which is infiltrated with round cells. The surrounding marrow is rich in hematopoietic cells. New bone has formed across the disk between D 2 and D 3 (Fig. 15c). Tuberculous granulation tissue containing epithelioid and giant cells is present in the anterior portion of the gap at the site of the kyphos.

COMMENT.—This case illustrates the pathologic changes brought about by both tuberculosis and osteomyelitis of the spine. These include extensive destruction of the fibrous and cartilaginous disks as well as of bone, and new bone formation and are as typical of pyogenic as of tuberculous infection.

Case 8.—W. P., male, age 8, was admitted to the University of Chicago Clinics February 18, 1931. This patient was first seen at the Home for Destitute Crippled Children in July, 1926, at which time a diagnosis of tuberculosis of the spine was made. In April, 1929, a psoas abscess and sinus developed which had continued to drain. In December, 1930, a diagnosis of amyloidosis and renal insufficiency was made.

September 17, 1931, the spine was fused with a rib graft. The patient recovered from the operation and for a few months there was improvement. Sinuses continued to drain, however, and approximately one year following the operation he died of amyloid nephrosis and uremia.

The diseased segment of the spine, from T 6 to L 5, was obtained at autopsy.

Pathology.—The sagittal section (Fig. 16a) shows osseous fusion of laminae and posterior spinous processes. The centra are reduced in their anteroposterior diameters. There is a kyphos in the lower thoracic spine. Collapse of the vertebral bodies from T 8 to T 11 has occurred but there is preservation of a portion of each intervertebral disk.

The centrum of T 9 is displaced backward so that it encroaches upon the spinal canal. The dura has not been invaded but a mass of débris can be seen extending downward anteriorly in the extradural space to the level of L 5. There is evidence of anterior invasion of the vertebral bodies from T 6 to L 4.

The roentgenogram of the split spine section (Fig. 16b) shows the previously described loss of substance of the centra of T 8, 9, 10, and 11, with partial preservation of the intervertebral disk spaces. The centra of L 1 and L 2 are firmly fused together and there is less complete bone union between L 4 and L 5.

The microscopic section includes six of the vertebral bodies (Fig. 17). The centra are reduced in size but do not show the usual wedging characteristic of extensive tuberculous invasion. The intervertebral disks show varying degrees of destruction and in places are bridged by new bone.

Some of the marrow is fibrous, but much of it is richly vascular and hematopoietic. Clumps of round cells and small abscess cavities are present in several of the centra. An occasional giant cell is visible in the pyogenic membrane lining the abscess cavities and a few tubercles, without caseous necrosis, can be identified.

COMMENT.—This case is complicated by the presence of the dual infection and presents features common to both tuberculosis and osteomyelitis. The loss of disk substance and bony coalescence in the lower thoracic and lumbar

FIG. 15a.—(Case 7) Age 19. Tuberculosis and Pyogenic Infection. Seven vertebrae of the thoracolumbar spine are included in the section. Only two disks (iv.d.) at each end of the section have been preserved. Remnants of other disks are represented by small islands of cartilage (c.c.). New bone trabeculae unite the vertebrae. A large abscess cavity (a.c.) is present at the level of the kyphos and two similar cavities may be seen beneath the anterior longitudinal ligament (a.l.l.). Invasion of an old disk space may be noted (a.) (×2).

FIG. 15b.—Section through the disk fragments at the level of the kyphos, showing cartilage islands (c.c.), abscess cavities (a.c.a.-a.c.b.), and the osseous fusion (n.b.) between adjacent centra (×10). Tuberculous granulation tissue containing epitheliod and giant cells is present in the gap at this level.

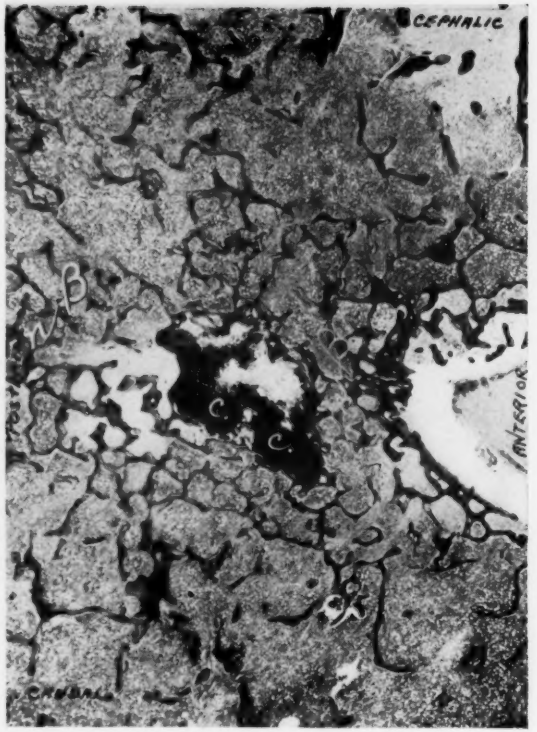

FIG. 15c.—A disrupted intervertebral disk at the distal part of the section. The only remnants of disk structure at this level are two small cartilaginous masses (c.c.) which have lost most of their cells and are partially calcified. Bone trabeculae (n.b.) have formed across the old intervertebral disk space (×10).

spine are more typical of pyogenic spondylitis. Preservation of considerable portions of the fibrocartilage of some disks where adjacent vertebrae have been markedly narrowed in their anteroposterior diameters, is more typical of an uncomplicated tuberculous spondylitis and indicates that the pyogenic infection was not extensive.

FIG. 16a.—(Case 8) Age 9. Tuberculosis and Pyogenic Infection. Photograph of the split section from T 6 to L 5. The kyphos (k.) is at the level of T 8. The collapsed mass of T 9 has been displaced backwards and encroaches upon the spinal canal (s.). The disk (d.) between L 1 and L 2 has been completely disrupted and the bodies have united.

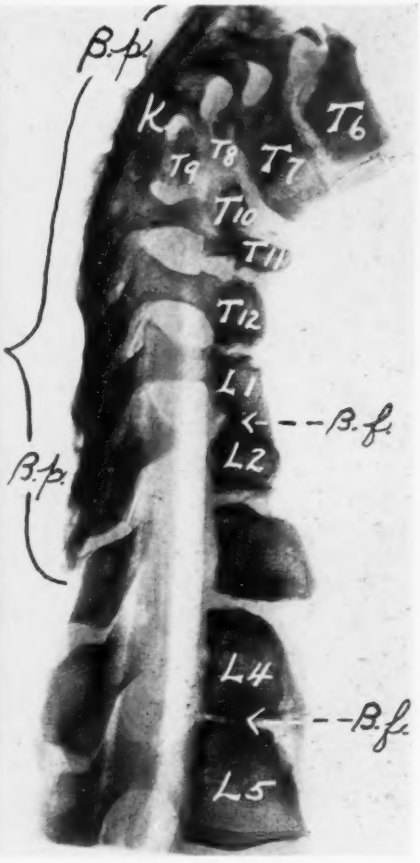

FIG. 16b.—Roentgenogram of split section. The bodies of T 8, 9 and 10 have been destroyed and form the apex of the kyphos (k.). Bony fusion (b.f.) is present between the centra of L 1 and 2 and L 4 and 5. The laminae from T 6 to L 2 are fused into a solid plate of bone (b.p.).

Case 9.—W. C., male, age 5. A diagnosis of tuberculosis of the thoracic spine was made in March, 1931.

There was moderate kyphosis and roentgenograms revealed a destructive lesion of the fourth, fifth and sixth thoracic vertebrae and a paravertebral abscess.

A two stage spinal fusion was performed on August 3 and August 19, 1931. The postoperative course was satisfactory and there was clinical and roentgenologic evidence of healing of the diseased spine. November 16, 1934, he was readmitted to the Clinics because of persistent high temperature of several weeks' duration. A paravertebral abscess was drained on November 21, 1934, with temporary relief of symptoms.

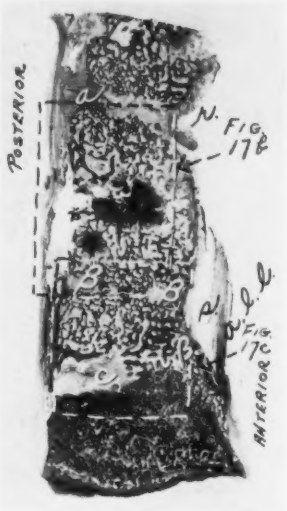

FIG. 17a.—(Case 8.) Age 9. Tuberculosis and Pyogenic Infection. This section includes six of the lower thoracic vertebrae. In only three areas (a.b.c.) may any disk structure be identified. Newly formed osseous tissue (n.b.) is growing through the anterior portion of the lower disk. The anterior ligament (a.l.l.) has been raised from the vertebral bodies by the migration of exudate and débris. Note the anterior invasion of a proximal disk (r.) and of a centrum (s.) (×2).

FIG. 17b.—The posterior end of a disrupted intervertebral disk (d.iv.d.) has been largely replaced by new bone trabeculae (n.b.). The posterior ligament (p.p.l.P) has been lifted from the centra by an abscess (a.c.) the walls of which are infiltrated with round cells and an occasional tubercle.

FIG. 17c.—Remnants of the hyaline cartilage and annulus of two disks (d.iv.d.). Newly formed bone (n.b.) unites the two vertebrae (×10).

Posterior mediastinitis developed and on January 14, 1935, drainage was established by incision through the eighth thoracic interspace. Streptococcus hemolyticus was grown in culture, and death occurred January 16, 1935. The abscess cavity extended along the front of the bodies of almost the entire thoracic spine. A segment of the spine from D 2 to D 12 was obtained at necropsy.

Pathology.—The bodies of T 4, 5 and 6 are triangularized and wedged, but show preservation of the anterior portion of the intervertebral disks (Fig. 18a). Only a small portion of the body of T 5 can be identified. Exudate and detritus elevate both the anterior and the posterior paravertebral ligaments, with surface invasion of the centra from the level of T 6 to T 11. The annulus of disk T 6–7 has been eroded from its dorsal aspect. The nucleus of disk T 7–8 has been destroyed. Disk T 8–9 has also been invaded. On the under surface of disk T 9–10, a part of the cartilage plate has been eroded by extension of a metaphyseal focus but the nucleus has not yet been extruded.

A roentgenogram of the split spine sections (Fig. 18b) shows fusion of the remnants of the bodies of T 4 and T 5. The erosion of the cortex of the superior and inferior surfaces of T 10 can also be recognized. There has been erosion of the posterior portion of T 8 and a similar change is noted on the distal margin of T 10 and on the anterior surface of T 11. The bone graft has been involved by the infection in its lower portion and presents a moth-eaten, necrotic appearance.

T 3 to a portion of T 9 is included in the first microscopic section (Fig. 19a). The remnant of T 5 is not shown. Intervertebral disks T 3–4 and T 6–7 are well preserved. The cartilage plates of disk T 8–9 have been eroded and much of the disk substance replaced by fibrous tissue and small abscess cavities. The contour of disk T 7–8 is preserved but there is invasion by newly formed bone trabeculae at the dorsal margin and a cyst-like area is shown at about the site of the nucleus pulposus. This area is lined with fibrous tissue, but the bone fragments and débris which fill it are artifacts from the sawdust made in splitting the spine (Fig. 19c).

The spongiosa of T 4 and T 6 is composed partly of old and partly of new trabeculae (Fig. 19b). Some of the marrow has been replaced by fibrous tissue in which scattered round cells, fibroblasts and small blood vessels may be identified. Isolated tubercles are visible in the centra of T 3, 4 and 6. The posterior paravertebral ligament has been lifted from the centra by the migration of an abscess which is lined by a pyogenic membrane.

Microscopic section (Fig. 19d) includes a portion of T 9 to T 12. A small abscess cavity lined with a pyogenic membrane is visible at the lower posterior portion of T 10. The cartilage is thinned beneath this cavity and the cortical bone has been absorbed. Another abscess is visible at this level, within the substance of the posterior ligament (Fig. 19e). The contour of all of the intervertebral disks at these lower levels has been preserved. None of the nuclei has been extruded or destroyed. The walls of the abscess cavities are infiltrated with round cells and polymorphonuclear leukocytes but no tubercles could be found in this section.

Comment.—Clinically, this case is one of acute vertebral tuberculosis which showed improvement following internal splinting and bed rest. Secondary infection from hemolytic streptococci led to abscess formation, mediastinitis and death. Preservation of intervertebral disks is marked when compared with the amount of osseous destruction. The pathologic and roentgenologic picture indicates that the pyogenic infection was acute and of short duration.

Discussion.—The current report by Finder[9] of extensive studies of the pathologic changes in the healing process in tuberculous spondylitis in a single adult patient has been reviewed. The findings which are shown in the published roentgenograms and photomicrographs of this case are quite similar

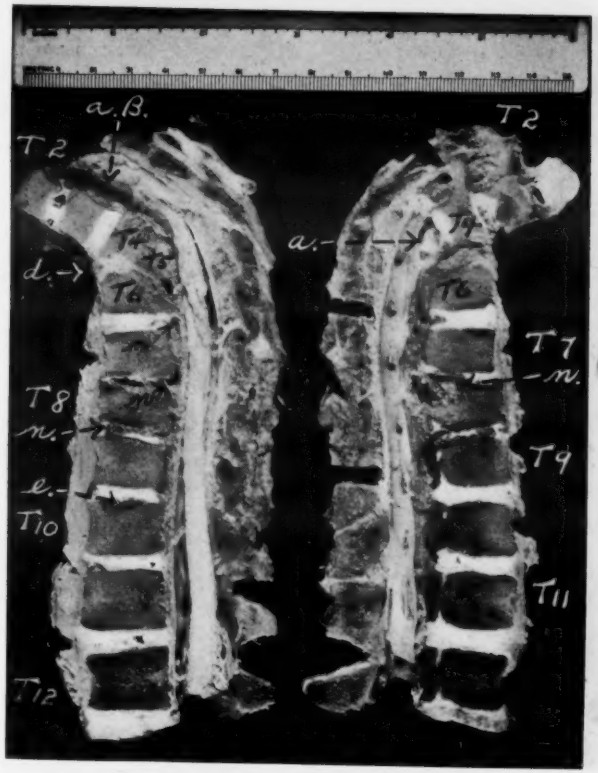

FIG. 18a.—(Case 9.) Age 9. Tuberculosis and Pyogenic Infection. Photograph of split spine section from T2 to T12. The bodies of T4, 5 and 6 are collapsed and wedged. The anterior portion of disk T5–6 (d.) is preserved, but its posterior portion is represented only by necrotic débris surrounding an abscess cavity (a.). A similar cavity (a.b.) is visible on the dorsal aspect of the bodies of T2 and 3. Three of the lower disks show invasion (n.) The cartilage plate on the superior surface of T10 is undergoing erosion (e.) from a subjacent metaphyseal focus.

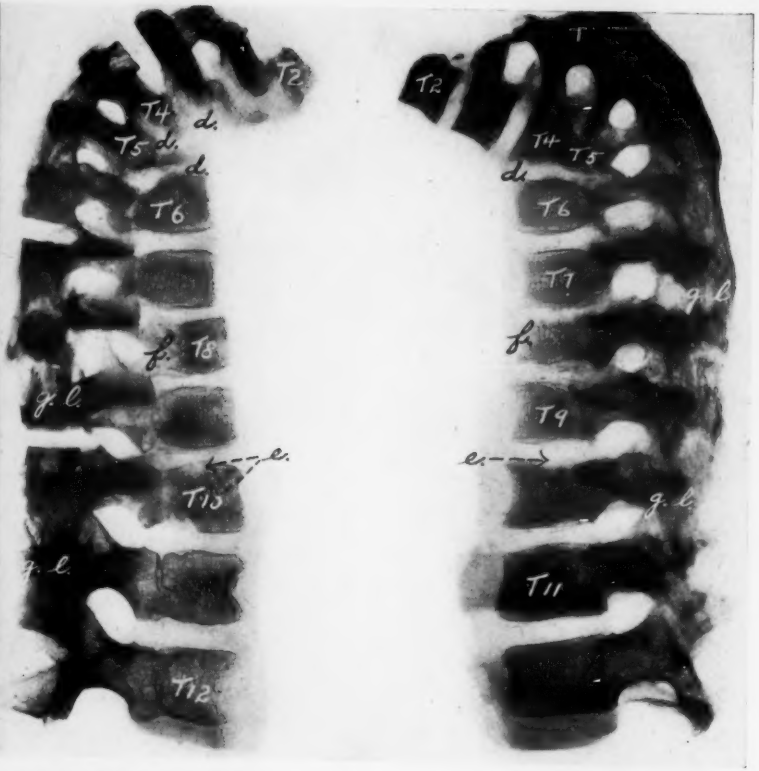

FIG. 18b.—Roentgenogram of split spine section. The bodies of T4, 5 and 6 are wedged and the intervening disks (d.) partially destroyed. There is beginning erosion (e.) of the upper surface of T10 and more extensive absorption and fragmentation of T8 (f.) The lower part of the tibial bone graft and corresponding lamina show extensive necrosis (g.l.).

FIG. 19a.—(Case 9) Age 9 years. Tuberculosis and Pyogenic Infection. T_3 to the upper fourth of T_9 are included in the section. The centra of T_4 and 6 have collapsed and show loss of spongiosa. T_5 was largely necrotic and could not be included. Several abscess cavities (a.c.) are visible in the section, some within the disk substance. The abscess cavity at the posterior level of the kyphos is lined with a pyogenic membrane (p.m.). The posterior ligament (p.p.l.) has been lifted from the vertebral bodies by exudate and débris (×2).

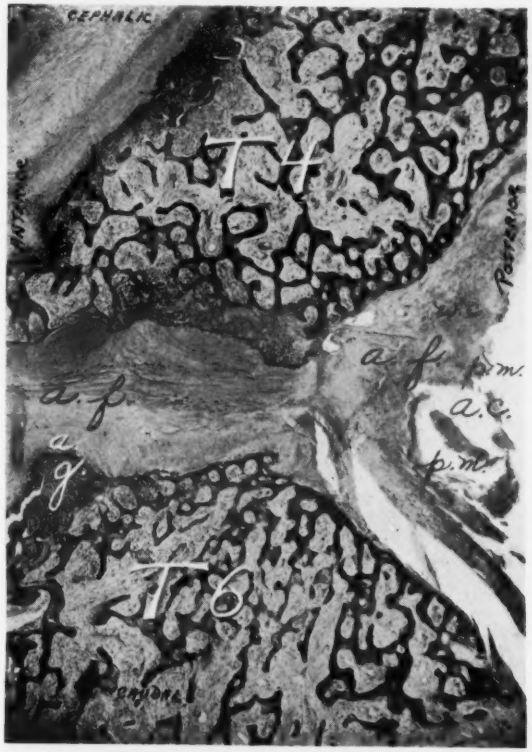

FIG. 19b.—This section shows the posterior margin of the intervertebral disk at the level of the kyphos. The annulus fibrosus (a.f.) is markedly thinned. There is beginning erosion of the intact remnant of the cartilage plate by tuberculous granulations (g.). The large abscess cavity (a.c.) is lined with a pyogenic membrane (p.m.), infiltrated with polynuclear leukocytes. Whorls of epithelioid cells with round cells but no giant cells (w.c.), can be seen in the posterior remnants of the annulus (a.f.) (×10).

FIG. 19c.—The cyst-like cavity in disk T_{7-8} (c) is lined with a pyogenic membrane (p.m.) and contains spicules of bone and "saw dust" from sectioning the spine. Newly formed bone trabeculae (n.b.) are shown invading the disk substance (×10).

to those of Case 7 of our series. In both cases there were multiple sinuses with secondary pyogenic infection, fusion of remnants of vertebral bodies and sclerosis of bone (less marked in our case). Active tuberculosis and abscesses were present. These findings are not those of healing uncomplicated tuberculosis, but can best be explained on the basis of the dual infection and are more typical of chronic osteomyelitis than of tuberculosis.

Tuberculosis of the spine commonly begins as a metaphyseal focus, and

FIG. 19d.—(Case 9) Age 9. Tuberculosis and Pyogenic Infection. The section includes T10, 11 and 12, with a portion of T9. Abscess cavities are visible at the level of disk T10–11, within the cancellous bone and in the posterior ligament (p.p.l.). The cartilage plate adjacent to the abscess cavity has been eroded (e). Anterior invasion of the centra of T10 and 11 may be noted at (a.) and (b.) (×2).

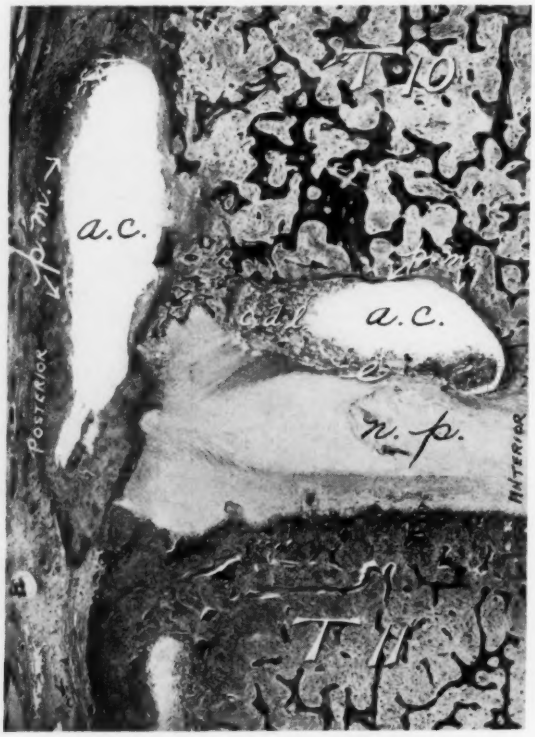

FIG. 19e.—Section through the abscess cavities at the level of disk T10–11. Both cavities (a.c.) are lined with a pyogenic membrane (p.m.) and partially filled with cellular débris and leukocytes (c.d.l.). The abscess at the disk margin has extended most of the way through the cartilage plate. The nucleus pulposus (n.p.) is still intact. This shows well the invasion of the bone first, followed by extension into the disk. No typical tubercles could be found in this section (×10).

the vertebral appendages are rarely involved. It is primarily a bone destroying infection and in the active stages of the disease there is little tendency toward bone repair which can be found either in the roentgenologic or pathologic specimen. The intervertebral disk, on the other hand, resists the tuberculous infection so that, as shown in some of the cases presented, the specimen may show extensive loss of several vertebral bodies with preservation of some of the cartilage and annulus of the corresponding intervertebral disks. The narrowing of the disk and the apparent thinning of disk space which

may be seen in the roentgenogram in comparatively early cases of tuberculosis of the spine may result from extrusion of the nucleus pulposus into disease softened osseous or ligamentous tissue.

Pyogenic infection is frequently primary in the arch or vertebral appendages. Early and complete destruction of the intervertebral disks is common. In contrast to tuberculosis of the spine, bone regeneration and fusion of vertebral bodies may be quite marked both in the roentgenologic and in the pathologic specimen. This rapid destruction of the intervertebral disk is accomplished by the proteolytic enzymes produced by the polymorphonuclear leukocytes in pyogenic exudates.

Tuberculosis of the spine spreads by extension of abscesses under the anterior longitudinal ligaments with surface invasion of the vertebral bodies anteriorly. The fibrous annulus of intervertebral disks that are in direct contact with the tuberculous abscesses show relatively little absorption while they are promptly destroyed by pyogenic exudate. In some cases there is hematogenous involvement of vertebrae at two or more levels.

Pyogenic infection may spread by direct extension through an intervertebral disk from vertebral body to vertebral body, but this manner of spread of vertebral tuberculosis has not been found in our studies.

Pressure on the spinal cord and the slow onset of spastic paralysis is more commonly caused by tuberculous spondylitis. Meningitis more commonly follows pyogenic osteomyelitis. Tuberculosis characteristically produces a slowly progressive deformity of the spine characterized first by a small knuckle or gibbus and later a kyphos which may result in the development of a "hunchback" dwarf. Pyogenic osteomyelitis does not produce extensive collapse of vertebral bodies and marked kyphosis.

Secondary infection of a tuberculous psoas abscess may produce pathologic and roentgenologic changes which are characteristic of osteomyelitis as well as the initial tuberculous infection.

Among infectious diseases, other than those caused by the more common pyogenic organisms, which may produce changes roentgenologically similar to those of spinal tuberculosis, are undulant fever, syphilis, and osteo-arthritis. Undulant fever is caused by an organism of one of the Brucella subgroups. Kulowski and Vinke[19] reported a case with involvement of the lumbar spine in which manual contact with suspicious infected cattle was the source of contamination. Archer[2] reported a case which was first diagnosed "Pott's disease." Other clinical reports of Malta fever spondylitis have been made, but no necropsy studies of human cases have been found in the literature (Guibal and Mas[12]). The disease is common in cattle and swine and results in abscess of the intervertebral body and the disk (Feldman and Olson[8]). Extension appears to be through the substance of the disk to invade the adjacent vertebrae.

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GIANT CELL TUMORS OF THE JAWS

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THE giant cell tumor is a comparatively uncommon lesion, and such a growth occurring in the mandible or maxilla is decidedly rare. The true nature of the tumor and its ultimate prognosis have occasioned wide variation of opinion during the past few years. Although giant cell epulis presents an histologic structure closely simulating that of the central giant cell tumor, the present discussion is concerned only with the latter.

In 1854 Sir James Paget[9] credited Lebert as being the first to describe the giant cell tumor. However, the history of the lesion really dates from the studies carried out by Nélaton.[21] He pointed out vividly the benignity of the neoplasm. The term "epulis" was coined by Virchow,[11] and unfortunately this poorly descriptive term has been handed down and is still in use today. The usage should be abandoned in favor of a terminology describing the nature, rather than the location, of the neoplasm. In 1837 Warren, of Boston, described benign and malignant forms of vascular erectile tumors of the maxilla, and in this group were probably included central giant cell tumors of the jaw. In the earlier surgical literature the term sarcoma was applied in designating the neoplasm, despite the work and careful observations of Nélaton. In 1910 the benign nature of the tumor was again emphasized by Bloodgood.[4] At that time he reported 18 cases, all of whom were still alive and well.

Unfortunately, as was the case with most bone tumors prior to the work of the Committee of the College of Surgeons for the Registry of Bone Tumors, numerous terms have been employed to designate this lesion. Nélaton knew it as tumeur à myéloplaxes. The term myeloid sarcoma was used almost universally from 1870 until 1910. The contradictory terminology of benign giant cell sarcoma gradually crept into common usage. The Committee for the Registry of Bone Tumors omitted giant cell sarcomata from its accepted nomenclature. As early as 1912 Bloodgood[5] designated this lesion as giant cell tumor, and this continues to be the accepted terminology.

The etiology of the so called giant cell tumor is still open to question. In general there are two prevailing opinions. The first would explain the lesion on the basis of an inflammatory reaction, whereas the second considers it as a true tumor. Barrie[3] considers it a hemorrhagic osteomyelitis, and the pathologic picture as a regenerative granulation process whose end effort is the restoration of areas already destroyed by some injurious factor,

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the etiologic agent responsible not having been ascertained as yet. Others would explain the causative agent on the basis of trauma. Whatever the opinion of a given investigator may be as regards the etiology of bone tumors, it cannot be denied that in at least some cases trauma would seem to play a part. Kolodny[19] believed that the effects of trauma, the regeneration and repair of tissues, the separation and isolation of cell complexes, hemorrhage with consequent absorption and encapsulation and the necrosis of tissue are all likely to play a part in the etiology of mesoblastic tumors, when brought together with certain predisposing factors. He believed it is probable that when a neoplasm makes its appearance immediately subsequent to trauma it is likely that the traumatizing agent merely accentuated the rapidity of the tumor growth. In the series reported by Simmons[24] a history of trauma was elicited in a high percentage of cases. Geschickter and Copeland[13] have elaborated a theory as regards the origin of giant cell tumor of bone which deserves special consideration. They considered it to be the end-result of an imbalance of two normal repair processes: an unusual increase in osteoclastic proliferation, and a diminution or a suspension of new bone formation in an injured cortex. The abnormal osteoclastic proliferation may occur as a phase in the histogenesis of intracartilaginous bone. In support of this hypothesis they contended that benign giant cell tumors develop at the sites where bone is formed from cartilage. The reasons given for the site of predilection for giant cell tumors at the epiphyses is the age of the patient, the common site of injury, the rate and extent of cartilaginous ossification at the end of the bone, and the nature of the blood supply. They contended that in the skull giant cell tumors occur only at sites where the bone is derived from cartilage, and does not form in membranous bones. Before accepting this theory the question should be raised relative to the infrequence for such lesions to arise about the seat of fracture, and about chronic bone infections, in which both phases of bone repair are prominent. Secondly, although the cartilaginous and membranous components of the mandible are ossified during the first year of life, the late appearance of a giant cell tumor of the mandible might be explained as being associated with the osteoclysis incident to shedding of the deciduous teeth. The author questions whether such a lesion would be centrally located, or would not tend to be of the so called epulis type. Kolodny[19] stated that although opinion is not yet definitely settled as to whether the lesion is a true blastoma, or merely an inflammatory process, the trend of opinion in recent years has inclined to the inflammatory theory. On the contrary, Stone and Ewing[26] have stated that the more aggressive and destructive cases are certainly neoplastic in character.

Giant cell tumors are of relatively infrequent occurrence. Exclusive of epulis arising from the alveolar borders of the jaws, the records of the surgical pathologic laboratory at Johns Hopkins Hospital over a period of 35 years showed 20 cases of giant cell tumor involving the jaws: six occurred in the maxilla and 14 in the mandible. In the Mayo Clinic series of 84 cases of giant cell tumor listed as to location, nine occurred in the maxilla

and seven in the mandible. Kolodny estimated that the relative frequency of this neoplasm to primary malignant bone tumor is one to two. It is generally agreed that giant cell tumor is a lesion of early adult life. Simmons[24] has given the decade of most common frequency as 20 to 30 years, and Geschickter and Copeland[15] estimated that 40 per cent of the cases occur in the third decade. Kolodny[19] found them to occur most commonly between 15 and 25. It is probable that giant cell tumors of the jaws tend to occur at a little earlier age than similar neoplasms of the extremities. Pfahler and Parry[23] thought that the mandible is one of the most common sites of this lesion.

There does not appear to be any special sex predilection. Simmons thought the neoplasms occur with slightly greater frequency in the female.

There are few symptoms produced by the presence of a giant cell tumor. The usual sequence given by Geschickter and Copeland[15] is: trauma, pain, tumor and fracture—all within two to 14 months. Kolodny,[19] on the other hand, considered the giant cell tumor to be of slow growth and of long duration. Pain is not a prominent feature of the condition. Holland[17] has spoken of rheumatic like pain during the development of the growth. Pathologic fracture is often the first symptom of the disease. In the jaws the tumor develops centrally and expands the cortical bone so that deformity can be detected relatively early. The expanded cortical shell often crepitates under the examining finger. The mucous membrane overlying this expanded shell is often dark red, or even purple in color. Tenderness on palpation is either slight or absent. The deformity is often pronounced and exhibits itself as a smoothly rounded mass, the junction of the expanded cortical bone with the normal bone of the jaw being smooth rather than sharply abrupt, as might be suggested by the roentgenograms.

The roentgenographic appearance of the giant cell tumor is characteristic. There is a bulky, roughly spherical or ovoid shadow, the margins of which are fairly definitely demarcated. The shadow is not smoothly circular in outline, but here and there presents small lobulations. There are incomplete trabeculae at the periphery of the tumor. There is no periosteal reaction, and the cortex and the periosteum beyond the tumor appear to be normal. The periosteum is never separated from the uninvolved bone, so that there is no so called reactive triangle. Sometimes the cortex has actually been eroded by the tumor. Kirklin and Moore[18] have expressed the opinion that there is a tendency for the tumor to break down the trabeculae and to form a conglomerate mass. They described a second roentgenographic type in which the growth may simulate the appearance of a metastatic tumor.

The true pathology of this group of so called tumors is but poorly understood. Geschickter and Copeland[15] have thought that the tumor begins subcortically and extends into the cancellous bone. The absence of periosteal reaction is characteristic. The growth is not primarily infiltrative, but expansive. The typical lesion consists of solid portions as well as numerous small cystic areas. The solid portions are friable, crumbly, granular masses, varying in color from yellow to dark red, but typically present the so called

currant jelly appearance. Extension into a joint cavity is extremely rare. Bloodgood described the general appearance of the tumor as simulating an old bruise. Sometimes fibrous areas may be palpated in the gross specimen, and occasionally the tumor is entirely encapsulated by fibrous tissue. The neoplasm may be easily scraped out of the bone cavity with a curette.

Microscopically the growth is found to be composed of large multinucleated giant cells loosely embedded in a stroma of smaller rounded, spindle and polygonal cells with large vesicular nuclei. The stroma is rich in various sized blood spaces; thin walled capillaries and newly formed blood vessels are not uncommonly seen. Geschickter and Copeland[15] estimated that under low power magnification there are on an average 30 giant cells per field, each with from 15 to 200 nuclei. The cell outline may or may not be distinct. Areas of hemorrhage are conspicuous, and the giant cells are most numerous about such regions, as well as about small cysts and spicules of bone. An attempt at organization of the hemorrhage may be apparent. The origin of the giant cells is still questionable. Some consider them to be derived from transformed wandering endothelial leukocytes; others think of them as hypertrophied bone cells which are liberated by the absorption of the bone matrix; others think them derived from modified endothelium; while Lubarsch is of the opinion that they originate from abortive vascular sprouts. In addition to the above components of the giant cell tumor, aggregates of endothelial leukocytes are present, filled with lipoid inclusions—the so called "foam cells."

It is a well known fact among pathologists that occasionally wide variance of opinion exists as to the microscopic diagnosis of this tumor. In general, in considering the diagnosis and prognosis of a bone tumor, the clinical, roentgenologic and the microscopic findings should be correlated, and too much reliance should not be placed on the histologic picture. It is generally conceded that there are many microscopic variants of the so called typical giant cell tumor. Kolodny has divided the tumor into four groups: simple giant cell tumor; xanthoma; the myxomatous type, and the telangiectatic type. He considered all four types as representing the same type of tumor, and believed the microscopic pathologic appearance to be of very little clinical significance. Stone and Ewing, as well as many other pathologists, have recognized various grades of malignancy in this neoplasm, noting zones of bone formation and the occurrence of very cellular areas of spindle cells. It is generally agreed that, from a microscopic standpoint, the malignant potentialities of a given tumor can be judged best by the appearance of the stroma cells. The character of the giant cells offers little aid in this regard. Although Stone and Ewing have recognized various grades of malignancy in these growths, they have not felt justified in including the atypical forms among the malignant osteogenic sarcomata.

The metastatic manifestations of giant cell tumor have raised some question as to its benignity. Simmons has stated that he has seen four cases in which death occurred from metastases of giant cell tumors. Coley[9] re-

ported 50 cases of this neoplasm, nine of which metastasized. Stone and Ewing, on the contrary, have stated that rarely, if ever, does a true giant cell tumor metastasize. They report one case in which they consider malignant change was due to repeated operative trauma. They called attention to the fact that there is no satisfactory record of metastasis of a giant cell tumor in its original form. Kirklin and Moore did not observe metastases in any of their cases.

As to the metamorphosis from a benign to a malignant tumor, there is again a division of opinion. Ashhurst[2] believed that after several recurrences the tumor may change its nature and become malignant. Chatterton and Flagstad[7] have observed the same phenomenon, even in cases in which the "trauma and operative interference have been mild." Simmons concurred. Coley[10] has stated that there is a one in five chance that a growth which appears to be a giant cell tumor from the clinical and roentgenologic evidence will prove to be malignant. Geschickter and Copeland[12] championed the benignity of the tumor, and state that benign giant cell tumor never develops into an osteogenic sarcoma. Malignancy developed in none of the cases reviewed by Kirklin and Moore.

The giant cell tumor seems to bear a definite connection to osteitis fibrosa cystica, although it is not clear just how intimate that relationship is. As Simmons and Kolodny[19] have shown, the older giant cell tumors show evidence of fibrosis, either as the result of advancing age, treatment, or fracture. Barrie considered the solitary bone cyst, osteitis fibrosa cystica and giant cell tumor as different phases of the same process—an attempt at repair following bone destruction. Geschickter and Copeland[12] have postulated that a bone cyst occurring in the metaphyseal region of one of the long bones of the young individual represents a healing phase of giant cell tumor—a conclusion based on clinical, pathologic and anatomic observations, and demonstrated by an analysis of numerous transitional lesions between these two entities.

This brings up the question of the correlation between the so called multiple giant cell tumors and parathyroid tumors. Alexander and Crawford[1] collected four cases from the American and seven from the foreign literature of multiple giant cell tumor. These authors quoted a communication from Codman in which he stated that he is skeptical about the existence of such a condition. Pfahler and Parry reported a case of what appeared to be a giant cell tumor of the mandible, and who later developed multiple bone tumors. Subsequently a parathyroid tumor was found. There were no biopsies of the bone tumors. Kolodny[19] has been of the opinion that in the apparent multiple giant cell tumors one is probably dealing with osteitis fibrosa cystica. Geschickter and Copeland[15] have cited the work of Jaffe in which this investigator showed that an experimental increase of the parathyroid hormone does not produce multiple tumors of the true giant cell type, although giant cell areas and osteitis fibrosa-like tissue may be formed in the bones of animals fed with an excessive amount of this substance.

Differential Diagnosis.—The giant cell tumor is an expansive type of growth, and must be differentiated from similar lesions occurring in the maxilla and mandible. The differential diagnosis of this tumor in the jaws is not different from that of the long bones, except in so far as several tumors indigenous to the jaws must be considered.

Dentigerous cyst occasionally offers some difficulty in the differential diagnosis. An unerupted tooth is always associated with the dentigerous cyst, and the cyst is unilocular with no trabeculae. However, sometimes a giant cell tumor may lie adjacent to an impacted tooth. In general, the outline or the dentigerous cyst is more regular, and most commonly is associated with an unerupted upper cuspid or with an impacted lower third molar tooth. The dentigerous cyst is lined with stratified squamous epithelium.

The radicular cyst ordinarily offers no great diagnostic problem, but there are cases in which the cyst attains large size and apparently loses its connection with the nonvital tooth from which it originated. The finding of vital teeth in the region of the tumor obviates the diagnosis of radicular cyst. This particular tumor is most commonly found in the upper lateral incisor area. The outline of this cyst is regular and is lined with stratified squamous epithelium.

The adamantine neoplasms are often quite difficult to differentiate from the giant cell tumors. Because of the trabeculation, the multilocular adamantinoma may simulate the giant cell tumor very closely. However, the adamantinoma is much slower in its development, the trabeculae are more clearly defined and usually extend throughout the tumor cavity, unlike those of the giant cell neoplasms, in which the trabeculations are often hazy and incomplete. If roentgen irradiation is employed it will be found that the adamantinoma is unresponsive, while the giant cell tumor quickly decreases in size under such treatment. The age of the patient and the location of the tumor do not offer much help, since both tumors occur in about the same age group and may occur in the same locations. Microscopically the adamantine epithelium is characteristic.

Osteogenic sarcoma offers diagnostic difficulty at times. However, in this tumor the periosteal reaction is usually evident, the reactive triangle of Codman is often present, the tumor is rapid in its development and microscopically most or all of the successive stages of bone formation may be demonstrable.

A central sarcoma, such as a fibrosarcoma, sometimes offers considerable difficulty, and often a microscopic section is necessary to differentiate the two conditions. The author recently operated a fibrosarcoma of the mandible in which the cortical bone was expanded but was still intact, there was no periosteal involvement, and the area of osteolysis simulated very closely that of a giant cell tumor. A biopsy, taken with the high frequency current, established the diagnosis, and jaw resection was done.

The giant cell tumor may resemble the lysis seen in a central carcinoma of the mandible, or may even resemble a carcinoma of the maxillary sinus.

Often the age of the patient will help to establish diagnosis, but occasionally a biopsy is required. In the opinion of the author, if the diagnosis rests between these two conditions, preoperative irradiation should be employed, despite numerous opinions to the contrary. If the lesion is of the giant cell type, marked diminution in its size will occur, whereas if the lesion is a carcinoma, the irradiation will render the malignancy more amenable to surgical therapy. The presence of a carcinoma of the prostate, thyroid or breast, or the establishment of a diagnosis of hypernephroma, will be of aid in ruling out metastatic carcinoma.

The giant cell tumor may sometimes be confused with a central fibroma. In the latter the growth is usually more tardy in its development, and the trabeculation is usually lacking. Fibro-osteoma should not be confused with giant cell tumor, since the lesion in giant cell tumor is entirely osteolytic in nature. Osteoma of the central type should offer no diagnostic difficulty. Multiple myeloma should not be confused with giant cell tumor and the uncommon solitary plasmocytoma of bone will rarely be mistaken.

Treatment.—The treatment of giant cell tumor has been revolutionized within recent years. Years ago amputation of an extremity, or resection of the involved area, was routinely advised. Although such therapy will undoubtedly give the greatest percentage of cures, it is by far too radical a procedure to be advised at the present time. Bloodgood[6] recommended resection only when such a procedure is made necessary by the complete absence of the bony shell, or when resection will leave the part with equally good function. Coates,[8] in a case of giant cell tumor of the upper jaw, has felt justified in maxillary resection for such a lesion.

At the present time the choice of treatment lies between curettage of the tumor bearing area, and roentgen irradiation, or a combination of the two. As early as 1910 Bloodgood[4] sponsored curettage followed by chemical cauterization of the cavity. This method is still in common use. The author prefers to cauterize with the high frequency current, and agrees with Peirce,[22] and others, in that roentgen therapy is always to be recommended following this procedure. Geschickter and Copeland[15] have stated that "curettement properly performed in carefully selected cases is unquestionably the treatment of choice."

Many able men recommend no surgery in the treatment of this growth, but advise roentgen irradiation alone. Herendeen[16] believed that most giant cell tumors can be cured by this method. Soiland and Costolow[25] obtained a complete response to roentgen therapy in every case. Pfahler and Parry[23] have thought curettement a disadvantage, and believed irradiation alone is definitely superior to surgery in the treatment of this group of tumors. Bloodgood, however, held that this method is more uncertain than curettement, is often more prolonged, and does not offer the advantage of a microscopic diagnosis in the doubtful cases. Geschickter and Copeland felt that postoperative irradiation of the tumor is of no particular advantage, and have stated that radium implantation has proved ill advised in the treatment of

giant cell tumors. A few investigators recommend the use of Coley's toxins in the treatment of the condition.

Prognosis.—If the tumor is left untreated it may reach tremendous proportions, and the patient may die from hemorrhage or from infection, without metastasis intervening. Kolodny[20] stated that occasionally, with no therapy whatsoever, either in the presence of a pathologic fracture, or without it, the tumor may be converted into a dry, firm fibrous tissue. In the center of such an area islands of active giant cell tumor may persist, although some such regions may degenerate and be replaced by cystic areas.

In 1919 Bloodgood[6] reported on a series of 47 cases treated by this method, with no recurrence. Herendeen[16] estimates that 25 per cent of the giant cell tumors recur after curettage. In a series of 105 cases treated by curettage, occurring in various parts of the body, Geschickter and Copeland[15] reported a recurrence in 31 cases. They[14] have considered the factors predisposing to recurrence as: patients over 35 years of age, advanced destruction of the bone shell, incomplete curettement, failure to use chemical or thermal cauterization subsequent to the curettage, and needless sacrifice of cortical bone at the time of the operation.

Case Reports

Case 1.—A girl, age 19, gave a history of seven months' duration. At the onset she noted a painless tumor in the canine fossa and several loose teeth in the upper left maxilla. She consulted her dentist and an upper bicuspid was removed. The tooth socket healed uneventfully. Because of the persistence of the loose teeth an exodontist was consulted. He performed a biopsy two months after the onset of symptoms, which was reported as granulation tissue, although giant cells were present in the section. Seven months after the onset the patient consulted the author. She presented a nontender mass in the left gingivobuccal fold which extended from the region of the upper left first molar to the midline. Marked bulging of the cortical bone was present over this area, with egg shell crepitation. The mucosa over the tumor was intact and was deep red in color. The left maxillary sinus was opaque on transillumination. The roentgenogram (Fig. 1) showed the presence of an osteolytic lesion of the left maxilla, with extensive involvement of the maxillary sinus. A tentative diagnosis was made of giant cell tumor. The blood Wassermann was negative, and the blood and urine examinations did not show any abnormality.

The mass was explored, after confirming the diagnosis by biopsy, the anterolateral wall of the maxillary sinus was removed, and about 200 grams of dark red, friable tissue were removed. The ethmoid cells did not appear to be involved. A sinus window was made in the lateral nasal wall, and the sinus was lightly packed with iodoform gauze because of hemorrhage. The patient was discharged from the hospital on the third postoperative day, and ten days later was referred for roentgen irradiation. Four weeks after operation the opening of the maxillary sinus into the mouth had completely closed. The upper teeth were later removed for cosmetic reasons. Figure 2 shows the roentgenologic appearance at the end of four months. There has been some bone formation. After two years the patient has had no further symptoms and no apparent recurrence of the tumor.

Case 2.—A woman, 23 years old, gave a history of very short duration. The tumor mass was discovered by her dentist a few days prior to her consulting the author. There had been no symptoms referable to the tumor. The past history was negative except that she had been hospitalized for study a year previously, and was discharged with a diagnosis of neurasthenia. There had been no symptoms referable to the jaws or teeth.

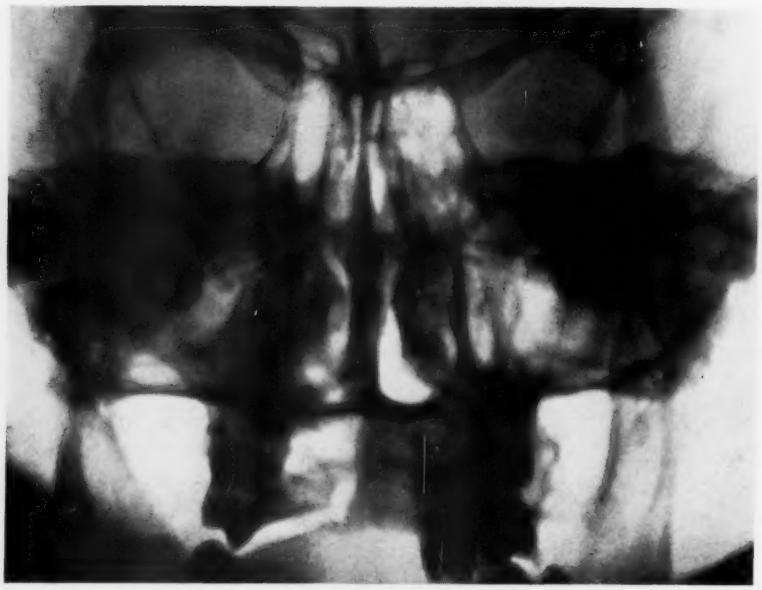

FIG. 1.—Giant cell tumor of the maxilla involving the maxillary sinus.

FIG. 2.—Same case as shown in Fig. 1. Taken four months following operation.

The patient was in a good state of nutrition and gave the general impression of being in rugged health. The blood calcium was 10 mg. per 100 cc. of blood and the serum phosphorus was within normal limits. The blood Wassermann was negative. R.B.C. 3,480,000, W.B.C. 7,000. Hemoglobin 72 per cent (Dare). The tumor mass extended from the region of the lower right first molar to the midline. The cortical bone on the buccal aspect was markedly expanded and egg shell crepitation was present. The mucosa was intact and was light purple in color. The roentgenogram (Fig. 3) presented the appearance of an osteolytic lesion, the lesion was irregularly lobulated, the trabeculae were scanty and incomplete, and there was no periosteal reaction. The diagnosis of probable

FIG. 3.—Giant cell tumor of the mandible.

giant cell tumor was made. At operation a horizontal incision was made in the lower gingivobuccal fold, the cortical bone thoroughly exposed, and after the diagnosis had been confirmed by a biopsy, the thin shell of cortical bone was removed, exposing the tumor bearing area. The field was easily visualized and the growth thoroughly removed. The cavity was loosely packed with iodoform gauze and the mucous membrane sutured with catgut. Two weeks following operation the patient was referred for roentgen irradiation. The patient made an uneventful recovery. Sixteen months after operation there has been no apparent recurrence of the tumor.

Case 3.—A boy, age 13, gave a history of a mass in the buccogingival region of the lower jaw of one year's duration. The patient had been told that he had a malignant inoperable tumor. There were no symptoms except those of a mechanical nature due to the size of the mass. On examination the patient appeared to be in excellent general health, and the tumor seemed to be causing no discomfort. A tumor mass presented in the buccogingival fold of the mandible extending from the region of the right first molar to the opposite cuspid. The mass was about the size of two tangerines placed side to side. The cortical bone was expanded, but the mucosa was intact over the tumor, pre-

senting a deep purple coloration. No tenderness was elicited on palpation. The diagnosis was made of a probable giant cell tumor. The roentgenogram (Fig. 4) revealed an osteolytic lesion extending from the region of the right bicuspid to the left cuspid, and the cortical bone was markedly expanded on its labial aspect. At operation the cortical bone was exposed as in Case 2; this was removed, and the tumor bearing area thoroughly curetted. Subsequent microscopic examination confirmed the diagnosis. The area was loosely packed with iodoform gauze and the mucous flaps sutured with catgut. The patient made an uneventful recovery and was referred for postoperative roentgen irradia-

FIG. 4.—Giant cell tumor of the mandible showing extensive expansion of the labial plate.

tion. Three years after the operation there has been no evidence of recurrence of the tumor.

The microscopic picture presented by all three cases was very similar, and can briefly be described as coming in the category of the "typical" giant cell tumor.

CONCLUSIONS

(1) An adequate explanation for the histogenesis of giant cell tumors has not been given.

(2) As regards the nature of the growth, certainly some, and probably all, are neoplastic in character.

(3) In a large percentage of cases the lesion should be diagnosed from clinical and roentgenologic data, and should be considered in the differential diagnosis in the doubtful instances.

(4) Biopsy should always be taken, preferably with the high frequency current, prior to removing such neoplasm. The tumor should be treated conservatively by curettage, followed by either chemical or thermal (high frequency) cauterization of the tumor bearing area.

(5) Roentgen irradiation of suspected giant cell tumors should not be advocated to the exclusion of surgery, since in certain cases the condition cannot be definitely differentiated from malignancy. The patient should receive the benefit of biopsy, and in case of malignancy the involved jaw should be resected. If roentgen therapy alone is advised, a certain percentage of

doubtful cases will succumb to malignancy, which surgery could have averted.

(6) Postoperative roentgen irradiation should be advocated in all cases.

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SUBCHONDRAL TUBERCULOUS SEQUESTRA

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THE subchondral wedge-shaped sequestrum in tuberculosis occurs with sufficient frequency to warrant a more thorough study of its significance. A number of writers have recognized the existence of this interesting formation, but no detailed studies were undertaken from the diagnostic or pathologic viewpoint. The American and British literature has been particularly deficient in this field, probably due to the difficulty of obtaining autopsy material. A review of the material seen in this clinic during the past six years is presented here, entailing a statistical analysis of cases recognized clinically from 1929 to 1934 inclusive. A detailed histopathologic study of 20 anatomic specimens served as a basis for a number of interesting conclusions regarding the formation of these subchondral tuberculous sequestra.

Definition.—The term sequestrum, as used here, denotes a subchondral focus of tuberculous necrosis which appears in the roentgenogram as a more or less wedge-shaped area of increased density. In contradistinction to sequestrum formation in nonspecific osteomyelitis, the tuberculous sequestrum does not necessarily lie "free" in the sense of complete dissection or separation from the surrounding bony tissue. Consequently, the roentgenologic diagnosis of tuberculous sequestrum is made with several reservations in mind.

First, the affinity of necrotic tissue, especially tuberculous caseation, for lime salts is well established. This is significant, because the necrotic tuberculous area, although of no greater density than the surrounding tissues, may cast a denser roentgenologic shadow due to precipitation of lime salts within the necrotic area (Fig. 1).

Second, simple necrosis of bone marrow and bony trabeculae will prohibit further resorption of bone in the necrotic focus, whereas the surrounding living bone tissue becomes porotic. Actually, there may be continuity of bony trabeculae from the subchondral necrotic area into the living epiphysis without signs of separation (Fig. 2). The porotic zone represents an area of collateral hyperemia with increased osteoclastic resorption. This again indicates that the roentgenologic sequestrum formation is only occasionally a true sequestrum. As a rule, it is but the contrast between denser necrotic trabeculae and porotic living bone.

Third, hypertrophic arthritis may confuse the picture. An arthritic focus, by virtue of its sclerotic bony trabeculae, may resist resorption for a longer period than the adjacent bone. This does not mean that the process of resorption of the sclerotic bone proceeds at a slower rate, but merely that at a time when the surrounding bone has almost disappeared, the arthritic focus still

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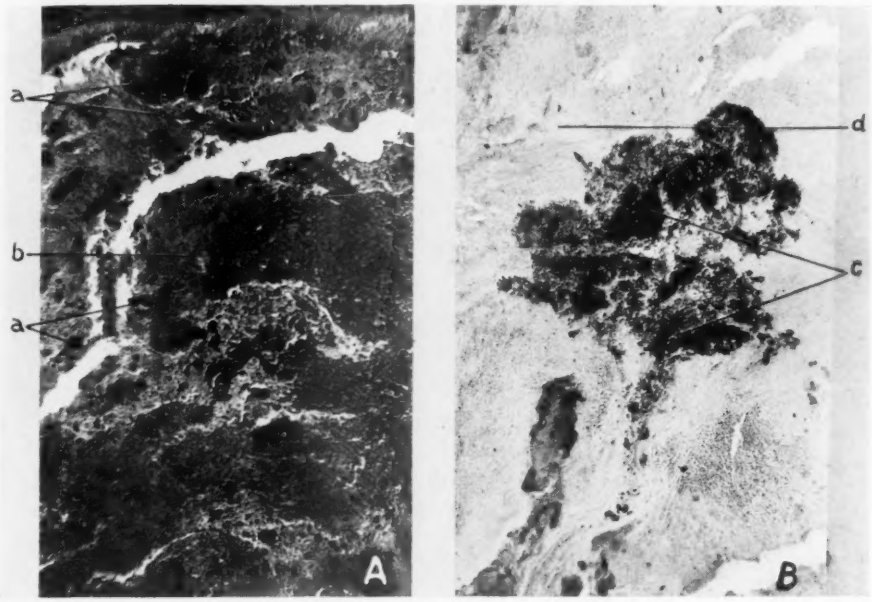

FIG. 1.—Both sections are taken from a tuberculous vertebra. A shows numerous small calcified bony fragments *a*, diffusely distributed in caseated material *b*. B is in the same magnification as A, but shows a more circumscribed precipitation of lime salts *c* in tuberculous caseation *d*. These areas would cast a denser shadow in the roentgenogram than the surrounding tissues.

has bone within it. The temporal element is quantitative, not qualitative. The roentgenologic picture of such an area may simulate a sequestrating focus (Fig. 3). Finally, the roentgenologic diagnosis of a wedge sequestrum is simple and absolute only when the focus is well separated and partially or wholly extruded into the joint cavity (Figs. 4 and 26).

Etiology.—Frequency: Before the days of the roentgen ray, Riedel[1] (1893) found sequestra in 45.2 per cent of 314 cases of tuberculosis (212 primary in bone, 102 primary in synovia) examined surgically. Menard[2] (1907), in 268 resections of tuberculous hips, discovered 87 joints (31 per cent) with sequestra, of which 81 appeared in the acetabulum, whereas only six sequestra were found in the femur, more in the neck and intertrochanteric region than in the head. In his article Menard stated that the surgeon required patience in searching for these sequestra. Garré[3] (1913), quoted by Hellner,[4] found 73 sequestra (8.5 per cent) in 849 instances of tuberculosis of the joints of the lower extremities. Sovetova[5] (1929) discovered only 69

FIG. 2.—This section demonstrates the continuity of the bony trabeculae *a*, which pass without interruption from necrotic bone marrow *b* to living fatty bone marrow *c*. The infection is oldest near the joint cavity *d*, and extends into the epiphysis by resorptive tubercles *e*.

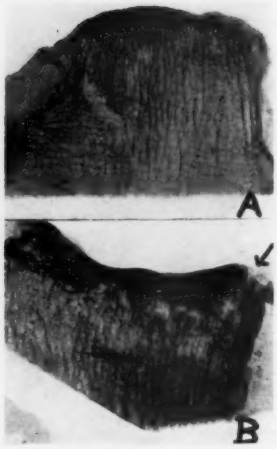

FIG. 3.—These roentgenologic positives of bone specimens indicate that an arthritic focus may simulate sequestrum formation due to the greater density of the sclerotic arthritic area. A shows a wedge-shaped focus bordering on the joint cavity with moderate porosis of the subjacent bone. The continuity of bony trabeculations rules out a true "free" sequestrum. In B the destructive process has apparently invaded the subchondral bone from the joint margin (note arrow) and has undermined the arthritic focus. The contrast between sclerosis and porosis is more marked, and the trabeculae seem to be interrupted in their continuity.

sequestra (4.1 per cent) in the routine examination of 1,443 roentgenograms of tuberculous joints. Hellner[4] (1930), in contrast to other observers, found only six of the larger isolated sequestra (1.7 per cent) in 346 cases of bone and joint tuberculosis.

The foregoing brief review shows that there is no conformity among the various observers in their statistics of frequency. In part, this may be explained by the difference in frequency with which various joints are affected. For example, an author who has a large number of hips in his series would have a greater incidence of sequestra than an observer who concentrated on other joints, especially those of the upper extremity. Of course, the ideal method is that which could provide anatomic and histologic confirmation of cases diagnosed clinically (roentgenologically), but unfortunately, such material is seldom available.

The statistics compiled herein include only cases which were seen in this clinic within five years of the onset of symptoms and which had had no previous surgical treatment. Ninety-one cases of joint involvement in 86 patients were available and acceptable for clinical study. Of 68 cases of proved

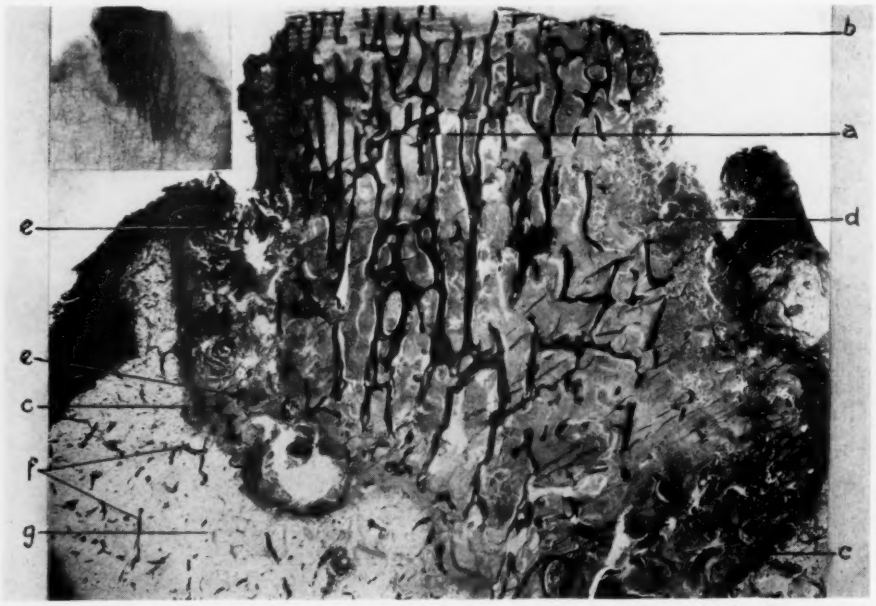

FIG. 4.—A well demarcated sequestrum *a* is being extruded into the joint cavity *b*. The zone of demarcation consists of tuberculous granulations *c*, necrotic débris *d*, and fragmented bone chips *e*. The contrast between the sclerotic necrotic trabeculae of the sequestrum and the extremely porotic living bone *f* in living fatty bone marrow *g* is marked. The inset depicts the roentgenologic appearance of this sequestrum.

FIG. 5.—(Case 33) Fungous tuberculous infection of the elbow in a 45-year-old male. A, after two years' duration of disease, shows a sequestrum of the lateral condyle of the humerus and of the coronoid process of the ulna. B and C were taken four months later and show better definition of the sequestra with separation of the ulnar focus.

tuberculosis, 21 had sequestra (31 per cent); there were ten sequestra (43 per cent) in 23 instances of unproved, but clinically certain, tuberculosis. Thus, 31 sequestra (34 per cent) were present in 91 joints. A comparative chart, showing the incidence of sequestra for each joint, as reported in the literature, is given in Table I. A number of sequestra are reproduced herewith by "positive" contact prints of their roentgenograms to illustrate the occurrence of subchondral sequestra in the various joints (Figs. 5 to 15 inclusive).

TABLE I

FREQUENCY OF OCCURRENCE OF SUBCHONDRAL SEQUESTRA ACCORDING TO JOINTS INVOLVED

Author	Riedel (1893) No Roentgenograms	Menard (1907) No Roentgenograms	Garré (1913) No Roentgenograms	Sovetova (1929) Roentgenograms Only	Hellner (1930) Roentgenograms and Specimens	Finder (1935) Roentgenograms
Shoulder	50%	...	...	...	...	25%
Elbow	31%	...	...	...	...	57%
Wrist	15%	...	...	...	...	0%
Hip	70.4%	31%	9.2%	...	...	50%
Knee	37.7%	...	5.5%	...	...	24%
Ankle	38.5%	...	7.5%	...	...	22%
Average	45.2%	31%	8.5%	4.1%	1.7%	34%

The presence of sinuses apparently had little bearing on sequestrum formation. Analysis revealed that sinuses occurred in 26 per cent of the cases in which sequestra were present, while 28 per cent of the cases without sequestra had sinuses. The tuberculous sequestrum formation, therefore, is apparently independent of secondary retrograde superinfection along a sinus tract, causing a complicating nonspecific osteomyelitis.

Pathogenesis.—The similarity of the wedge-shaped focus in subchondral bone tuberculosis to the wedge- or triangular-shaped infarct seen in parenchymatous organs has led many authors to consider the wedge-shaped sequestrum as a form of bony infarct, due to vascular occlusion. The publication of Koenig[6] (1896) stated that all oval or cone-shaped areas of necrosis were to be regarded as evidence of embolism; clumps of tubercle bacilli, alone or within tuberculous débris, lodged in end arteries of the epiphysis and infected the areas supplied by the obstructed vessel.

In 1912, Fraser[7] experimentally injected lampblack into vessels of the epiphysis. He found that triangular areas were colored in those joints where there was a connection between the blood vessels in the capsule and those in the substance of the surrounding bones. He believed, therefore, that primary vascular infection developed at the site of synovial reflection and entrance of vessels. This was mainly the case in the lower extremities. There was no

FIG. 6.—(Case 12) A sequestrum is present in the lateral condyle of the humerus of a 57-year-old male after 21 months' duration of the disease.

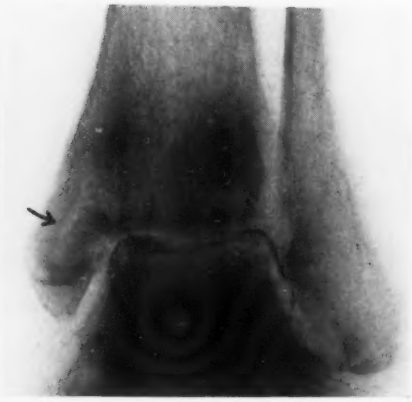

FIG. 7.—(Case 6) A 62-year-old female presented a sequestrum of the articular aspect of the medial malleolus only four months after the onset of symptoms.

FIG. 8.—(Case 39) A 21-year-old female showed a tuberculous sequestrum in the medial portion of the femoral intercondyloid notch after 13 months' duration of the disease.

FIG. 9.—(Case 31) Sequestration was noted in both condyles of the femur of a 23-year-old male, whose symptoms were present for three years. The medial sequestrum (black arrow) is being extruded into the joint cavity after four and a half years. The lateral sequestrum involves almost all of the articular surface of the condyle. Its resemblance to a calcified semilunar cartilage is ruled out by the continuity of bony trabeculae into the sequestrum. Both areas were demonstrable at operation.

particular site of election in the bones of the upper extremity, since there was but little connection between capsular and osseous vessels.

In 1923, Nussbaum[8] showed that the arteries of the epiphyses, unlike those of the metaphyses, are not end arteries. This concept is now generally accepted and refutes Koenig's assumptions. One year later, Phemister[9] showed quite accurately that tuberculous invasion develops mainly from the joint margins; he ascribed this process to a pressure effect, or rather to a lack of protective pressure at the nonweight bearing margins.

Although these theories differ in their views as to the mechanism of infection, they generally recognize that invasion most frequently chooses the joint margins as the site of predilection. While a combination of the mentioned factors may be responsible, it also seems reasonable to assume that secondary tuberculous infection of bone starts at the joint margins because the actual physical resistance there is decreased. In this region the joint cartilage is of slight thickness and the bony epiphysis is covered by only a thin layer of periosteum and synovia. This thin protecting membrane can be destroyed easily, permitting resorption of cortex and infection of bone marrow.

FIG. 10.—(Case 20) The upper pole of the head of the femur in a 20-year-old male presents a large sequestrum. Duration of the disease was two years.

It is well known that the marginal portion of a joint, especially the knee, forms a site of lessened resistance. In suppurative processes, or in any form of arthritis combined with increased intra-articular pressure, these areas become affected first. They yield to increased pressure by bone resorption, which gives the characteristic eroded foci seen in the roentgenogram (tuberculosis, hemophilia, suppurative arthritis, etc.).

A second site of predilection in this series occurred in areas showing arthritic changes. This is in contradiction to the statement that hypertrophic arthritis is a protection against tuberculous invasion. This conclusion was drawn after examining microscopically tuberculous specimens obtained from autopsy material of persons of advanced age, in whom the incidence of hypertrophic arthritis was relatively frequent. Two reasons for this predilection suggest themselves: first, these areas usually lack the protection of joint cartilage; second, constant mechanic irritation in these regions probably decreases the resistance of the bone marrow to tuberculous infection.

The protective rôle of joint cartilage was mentioned already in connection with infection invading bone at the joint margins. Thus, it is quite possible that while no signs of specific infection are seen in those areas where the joint cartilage acts as a protective barrier against bone invasion, tuberculous infec-

tion may be already advanced in areas of subchondral sclerosis (arthritis deformans), which lack the protection of a cartilaginous cover.

The accessibility of the spongy bone in areas surrounding a sclerotic, hypertrophic arthritic focus, combined with mechanic irritation and weakening of the spongy bone, makes invasion of the tuberculous granulation tissue relatively easy. At first, necrosis of bone and bone marrow leads to a rather sharp demarcation from the living tissues, but without true separation (Fig. 3). However, extensive caseation may result in sequestration of the necrotic area. In such cases, the bony tissue, which is dense, shows irregular outline of the trabeculae. Its density contrasts strikingly with the porotic surroundings. The density is due partly to sclerosis of arthritis and partly to necrosis of bone before resorption could progress very far. The surrounding porosis

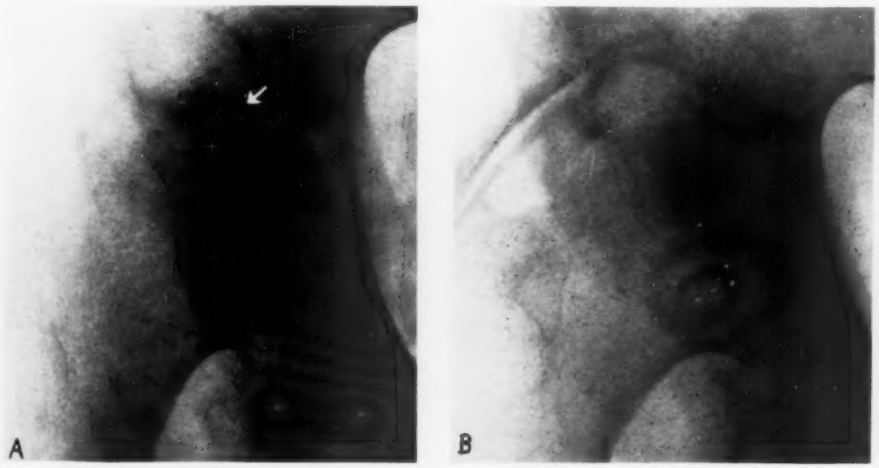

FIG. 11.—(Case 11) Symptoms were present for two years in the hip of a 27-year-old male. The white arrow in A points to a sequestrum, which stereoscopically lies behind the head of the femur. The origin of this sequestrum is marked by the acetabular defect above. B was taken three months later (two months after an extra-articular fusion of the hip). The acetabular sequestrum has become resorbed or is now overshadowed by the large area of necrosis involving the head.

is directly due to resorption by tuberculous granulation tissue. Therefore, the density of these areas in the roentgenogram cannot be taken simply as an expression of necrosis of bone tissue; the arthritic factor must also be evaluated. In some cases, gross inspection, as well as the roentgenogram, reveals a very dense focus of bone tissue separated from the otherwise markedly porotic joint end by a zone of dissection; the focus may separate enough to protrude considerably into the joint cavity (Fig. 4).

The development of a wedge-shaped focus of necrosis, according to most authors, requires at least three months from the time of onset of the infection until a roentgenologic diagnosis can be made. At least ten weeks are necessary for metaphyseal emboli-formed sequestra to become recognizable. The upper limit is unknown, but these foci may form after many years. The rate of disappearance of the wedge-shaped sequestrum is still more problematic. Kisch and Grunert[10] report a case in which the sequestrum disap-

FIG. 12.—(Case 8) A 14-year-old female had had symptoms for one year when A was taken. It shows early demarcation of an acetabular sequestrum. B, taken after ten months of immobilization, shows increase in size of the area of necrosis. Four months later, C shows no significant changes from B.

peared gradually within 14 months after iodine by mouth, heliotherapy and hyperemia were instituted. Several cases, followed in this clinic, furnished good roentgenologic evidence of development and disappearance of sequestra (Figs. 12, 13, 14 and 15).

Trauma, erosion and molecular disintegration may lead to wearing down of the sequestrum in the form of tiny sequestra or bone sand. In other cases, the sequestrum may be extruded into the joint cavity or into a sinus tract, leading outside the body. Sequestra which become encapsulated may be protected from further resorption and so remain unchanged indefinitely.

Histopathology.—Contrary to the usual concept that tuberculous infection of joint ends is primary in the bone, the specimens studied in this series showed secondary bone involvement in all cases, except four. This may be

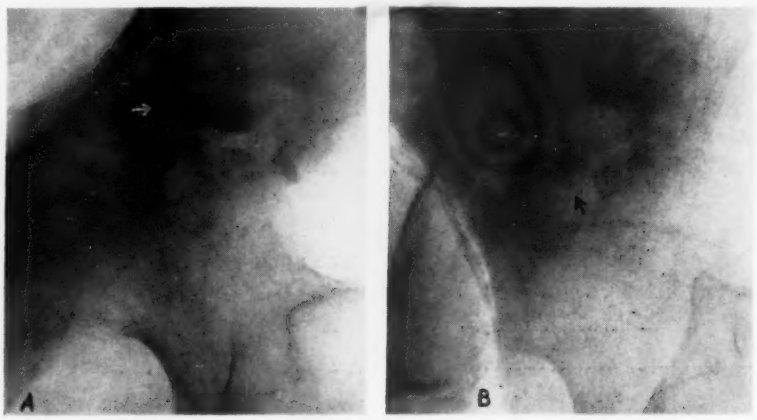

FIG. 13.—(Case 22, Figs. 13, 14, and 15) This series, occurring in a 24-year-old male with symptoms of six months' duration, demonstrates the possibility of disappearance of sequestra. After six months A shows a well demarcated acetabular sequestrum. After ten months the sequestrum, as seen in B, has dropped somewhat and is lying free in the joint cavity.

due to the fact that the histologic material which was derived from individuals of advanced age may give a distorted picture; it is possible that in younger persons the primary bone infection might prevail. However, the question of primary or secondary bone involvement can be settled only by studying material in which the disease was of relatively short duration. When the disease is of longer standing, it is possible that a primary bone involvement may break into the joint, where a secondary tuberculous arthritis develops. The process may then become widespread and reinfect the bone tissue. On the whole, such material would be unsatisfactory for accurate determination as to whether bone invasion was primary or secondary.

Primary Bone Involvement.—Primary subchondral bone tuberculosis presents certain histologic differences from the more frequent secondary form. In earlier cases the focus of infection is more centrally located within the epiphysis; the subchondral marrow spaces are fairly well preserved. Subsequently, the latter may become involved also, but they show signs of more

recent infection and bone resorption. These findings speak against primary vessel occlusion and resultant infarct type of necrosis.

The only instance which suggested the possibility of a vascular involvement as the cause of necrosis was seen in a case where the marrow spaces

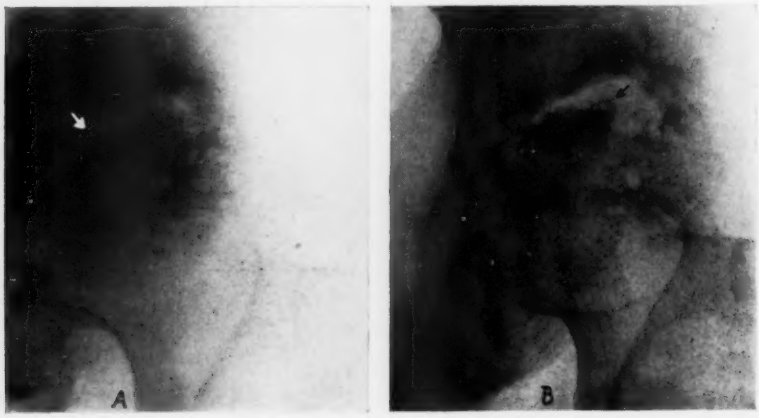

FIG. 14.—(Case 22, continued) In A the sequestrum seems to be smaller, after 15 months. In B, after 18 months, the sequestrum lies behind the head of the femur.

were involved more extensively by necrosis than by invasion of tuberculous granulations. The involved focus was more or less triangular-shaped, and at the apex an artery, vein and enlarged lymph sinuses could be seen (Fig. 16). Lymphocytic infiltration was increased around these vessels; the wall of the

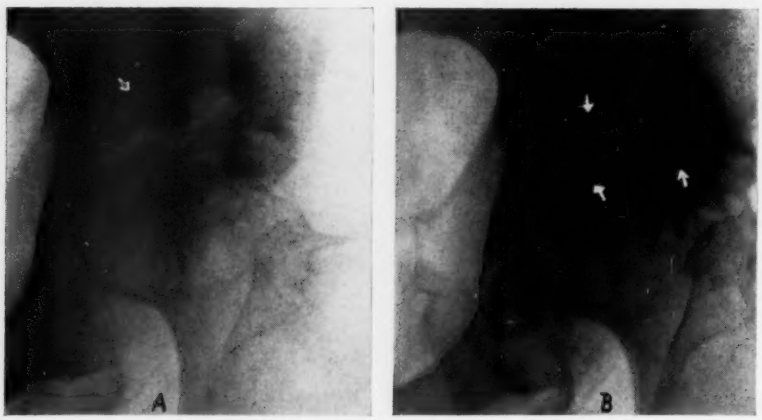

FIG. 15.—(Case 22, continued) Twenty-eight months after onset of disease, A reveals the relatively small remains of the original sequestrum (black arrow). A new, secondary area of necrosis (white arrow) is being sequestrated from the acetabulum. A small focus seems to be developing in the superior lateral pole of the femoral head. This focus is confirmed in B, taken after 52 months. The changes in the acetabular sequestra seem to be at a standstill.

artery was edematous, but not infiltrated. The infection of the joint most likely extended along the lymph vessels into the deeper marrow spaces, apparently leading to a toxic necrosis, rather than an aseptic necrosis of bone marrow by vessel occlusion.

This instance of subchondral necrosis, whose configuration suggests a wedge sequestrum, can be attributed to propagation of infection along vessels. It must be conceded, therefore, that the wedge sequestrum of tuberculous necrosis may be the result of preformed anatomic structure. As a rule, however, the tuberculous necrosis, primary or secondary, is not related to primary vascular alterations.

The primary infection, which develops within the epiphysis, invades the surrounding tissues centrifugally in the form of resorption tubercles. As reactive changes occur in the living tissue bordering on the original epiphyseal focus of bone infection, walling off may be initiated by a tendency to fibrous

FIG. 16.—The possibility of a "bone infarct" due to vascular involvement is sometimes demonstrable. At the apex of the wedge-shaped area of necrosis *a* are an artery *b*, vein *c*, and lymph sinuses *d*. The necrosis, which extends fan-like towards the joint cavity *e* is probably toxic, independent of tuberculous granulations.

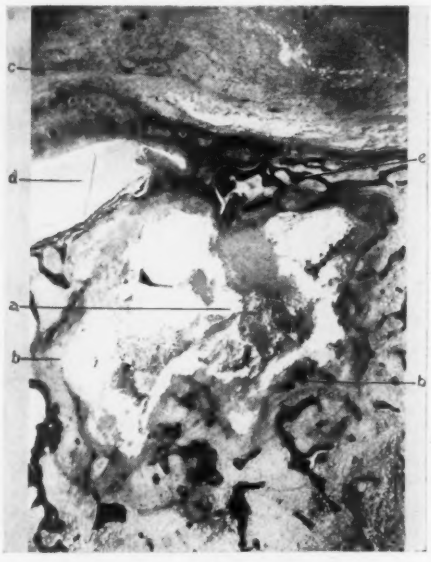

FIG. 17.—The subchondral abscess *a*, whose wall is lined by tuberculous granulations *b*, is in connection with the joint cavity *c* through an isthmus between the junction of marginal joint cartilage *d* and cortex *e*. The joint, which is already filled with tuberculous caseation, may have perforated the bone at this point, leading to abscess formation. On the other hand, the abscess, even though secondary to the joint infection, may have developed as a separate focus, and is now about to break into the joint.

condensation along the borderline of granulation tissue between living and necrotic bone tissue.

As the tuberculous process extends, the infection ultimately reaches the joint cartilage; this barrier impedes its progress in a centrifugal direction toward the joint cavity, but permits spreading of the disease along the subchondral bone marrow spaces. Thus, the tendency to check dissemination in the more central portions of the epiphysis, where the infection is older, while the subchondral spreading is still active may lead to the formation of a sequestrum whose shape is more or less of a wedge. The definitive shape apparently depends upon the speed with which walling off occurs at the pri-

mary site: if it is rapid, a fairly sharp apex should result, giving a triangular form; if the process is slower the apex will be wider and a wedge shape is assumed.

As the infection spreads subchondrally, the cartilage eventually may be resorbed from below, allowing the infection to break into the joint cavity. The joint invasion may be preceded by abscess formation in the subchondral marrow spaces, which become filled with tuberculous pus and necrotic bony trabeculae. The wall of the abscess is formed by tuberculous granulations, but there is not true sequestrum formation. Finally, the abscess breaks into the joint, frequently selecting the margin of joint cartilage and cortex, leading to a secondary tuberculous arthritis (Fig. 17).

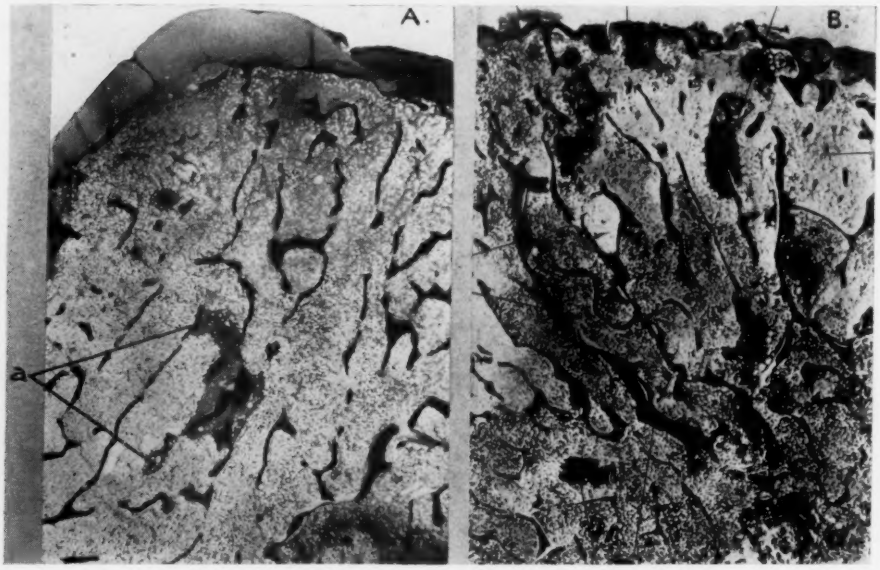

FIG. 18.—The tuberculous infection is seen spreading by continuity along the paratrabecular lymph sinuses *a* into the epiphysis. This is similar to the dissemination in B, which is taken from a case of suppurative arthritis with secondary osteomyelitis (after Freund[11]).

Secondary Bone Infection.—Tuberculous subchondral necrosis most often is due to secondary invasion of bone marrow from an extensive joint infection. Ordinarily, the infection from the joint spreads through the openings between the bony trabeculae by continuity. The infection follows along the margins of the trabeculae, very similar to the invasion in a suppurative process (Fig. 18). Necrotic bone marrow with large fat holes may surround several long living bony trabeculae, which still show a preserved nuclear stain. As Freund[11] has shown in his study of secondary nonspecific osteomyelitis of the epiphysis, joint infection may follow lymph sinuses along the endosteal surface of the bony trabeculae (Fig. 18).

The spread of infection and tuberculous granulations in the subchondral zone leads to destruction of cartilage from below, although the more distal cartilage may remain fairly well preserved. As the granulations accumulate

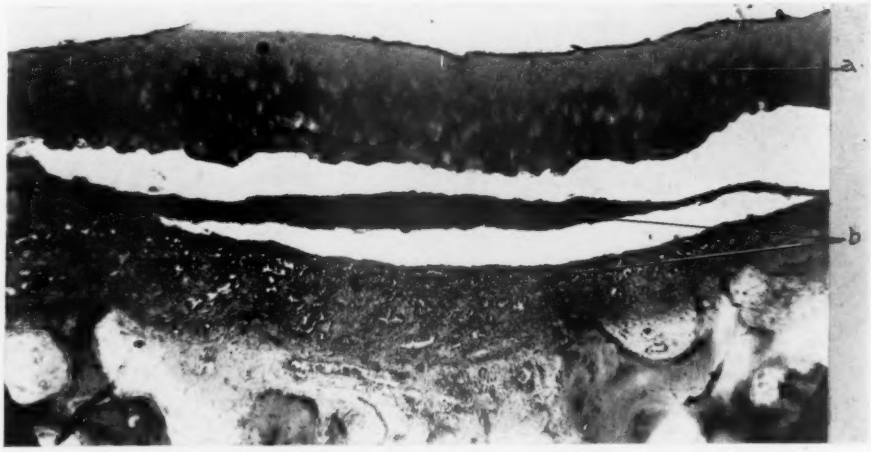

FIG. 19.—The joint cartilage *a*, although undermined by tuberculous granulations *b*, is still fairly well preserved down to its calcified layer. The dissection of the cartilage from below has resulted in its complete desquamation.

FIG. 20.—The advance of the infection into the subchondral bone is marked by a zone of resorptive tubercles *a*, which sharply demarcate the necrotic bone *b* from the living bone *c* and fatty bone marrow *d*, deeper in the epiphysis. The superficial layers of tuberculous granulations *e* have undergone necrosis *f*, especially bordering on the joint cavity *g*, where the process is oldest.

they may dissect the overlying cartilage, often including the calcified layers, from the subchondral bone, so that a relatively large portion of joint cartilage may desquamate (Fig. 19).

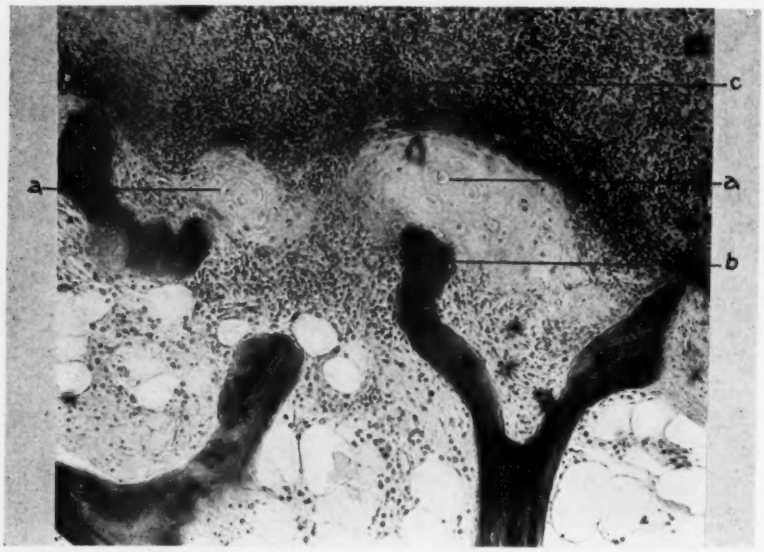

FIG. 21.—The fibrous cartilaginous caps *a* overlying the bony trabeculae *b* represent an attempt at regeneration of a new joint cover after destruction of the original cartilage by invasion of tuberculous granulation tissue *c*.

The underlying exposed marrow spaces become filled with caseated material, and by confluence of several necrotic foci a large area, simulating a

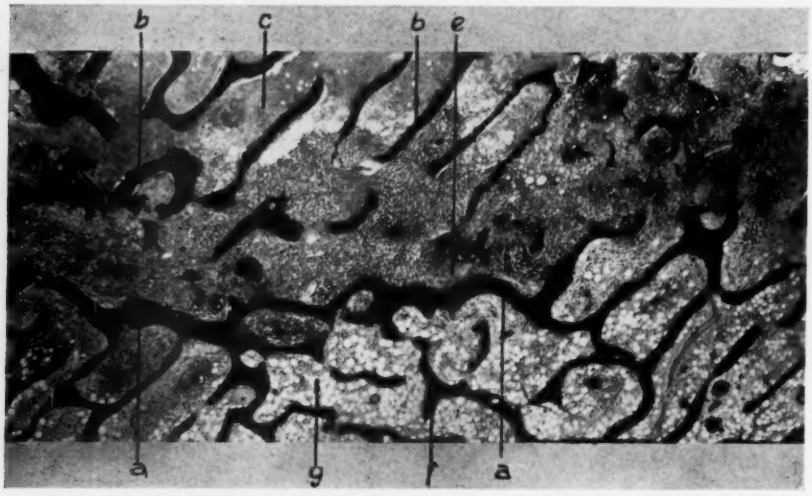

FIG. 22.—The bony trabeculae have formed a transverse lamella *a* in an attempt to halt the spread of infection into the epiphysis. Towards the joint the necrotic bony trabeculae *b* lie in necrotic tissue *c* and tuberculous granulations *e*; towards the epiphysis the bony trabeculae *f* are alive in fatty bone marrow *g*.

wedge, may result. However, the shape of sequestra more common to secondary bone involvement resembles a trapezoid or butterfly. That the

wedge shape is more or less accidental can be seen in some cases, where caseation of subchondral bone marrow occurs over a fairly large area, but the extension deeper into the epiphysis is rather localized.

The demarcation of the necrotic area is usually represented by a zone of tuberculous granulations, which is the advance zone of infection (Fig. 20). In the active early stages there may be a fibrinous exudate, which contains a great many epithelioid cells and is in firm connection with the tuberculous granulations, which show a great number of epithelioid and giant cell tubercles. Tubercles are also found in the bone marrow, beyond the zone of granulation tissue. Osteoclastic bone resorption is greater there, and the nearby marrow spaces show marked hyperemia, edema, and cellular infiltration. Plasma cells and lymphocytes predominate, probably as a response to the specific infection. Not infrequently, the interposed zone of tuberculous granulation tissue is loaded with small fragments of bony trabeculae, which frequently show nice examples of bending and splitting of lamellae on their convex sides. This zone, however, does not effect a distinct dissection of the infected necrotic area.

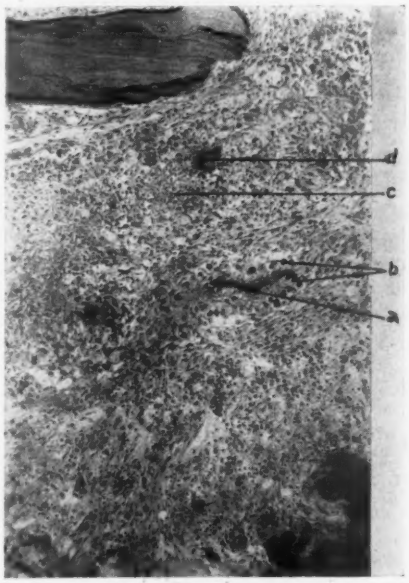

FIG. 23.—Osteogenesis on a fibrous tissue basis may occur even in the presence of active tuberculosis. Osteoid tissue *a* is seen surrounded completely by a layer of osteoblasts *b*, although only separated by a few micra from a tubercle *c* containing a Langhans giant cell *d*.

As the granulation tissue grows older it develops a fibrous condensation. The fibrous wall may form a protective barrier for the underlying marrow spaces against further invasion from the joint cavity. This fibrous tissue may even develop new cartilaginous islands over prominent bony trabeculae, where gliding occurs (Fig. 21). Such cartilage formation represents an attempt to regenerate a cartilaginous joint cover; it is interesting that it may occur despite the presence of active tuberculosis.

In cases of extensive tuberculosis of the fungous type, the subchondral involvement may be very gradual and without apparent foci of marrow caseation. This form has to be differentiated from the more frequently observed type described above, where rather large areas of secondary bone tuberculosis have developed.

An uncommon type of separation is characterized by the formation of demarcating bony lamellae which sharply separate the sequestrum with its surrounding tuberculous granulations from the noninvolved bone marrow spaces (Fig. 22). These demarcating bony laminae are the result of a complex process of bone apposition and bone resorption taking place on the sur-

face of bony trabeculae. The structure of the bony trabeculae is also complex, and consists of many dark blue, lacunar cement lines which separate old (sometimes necrotic) bone tissue from the new living bone. Some bone also develops simply on a fibrous tissue basis with osteoid and osteoblasts; this occurs within the tuberculous granulation tissue despite the presence of tubercles (Fig. 23).

In addition to demarcation of necrotic from living bone by caseous material, granulation tissue, fibrous tissue or bony lamellae, it is possible to find separation effected by trauma. The mechanic resistance of the joint end is materially weakened by the invading infection, so that by relatively insignificant injury a marginal portion (as in the femoral condyle, for example) may be broken off. This is illustrated in places where a zone of separation, without any interposed tuberculous granulation tissue, can be found extending straight through necrotic bone toward the joint surface. This space represents an intra-articular fracture line (Fig. 24).

Necrosis.—The extent to which changes develop in necrotic or sequestrated bone tissue is largely dependent upon the rapidity or slowness with which death of the bone marrow and bony trabeculae occurs. If the advancement of the tuberculous process is gradual, then reactive changes as they occur in living bone tissue should also be manifest in the necrotic areas in the form of bone resorption.

Quite typically, a region gradually invaded by tuberculosis shows subchondral bone denuded of joint cartilage and covered by a zone of tuberculous granulations, whose superficial layers characteristically undergo necrosis (caseation). The deeper layers (at a greater distance from the joint cavity), however, are extremely rich in tubercles, some of which have fibrous capsules. The bone tissue included in this area has undergone extensive resorption and is lacunar in outline. The other portions of the epiphysis show a considerable degree of osteoporosis, which is most marked in the affected area. By progression of the tuberculous infection an extensive portion of the epiphysis may become overrun and undergo caseation. Here, too, tuberculous granulation tissue marks the advance of the invading infection. The bony trabeculae in the demarcated area of necrosis show more or less marked signs of bone resorption, depending on the celerity with which the infected area became necrotic. Thus, this process may lead to demarcation and sequestration of extensive areas without presenting primary tuberculous joint sequestra.

The bone marrow and trabeculae of a sequestrum which has been demarcated by a rapid infectious process does not have time to undergo reactive changes. As a consequence, the bony tissue is practically of the same density throughout the entire sequestrated or necrotic area; bone resorption is almost entirely absent; and the margins of the trabeculae are relatively smooth. The surrounding necrotic areas, however, display different stages of destruction, and the trabeculae in these areas show corresponding variations in density. If the density of the trabeculae of the sequestrum is approximately

the same as that of the surrounding bone tissue, it may be assumed that the focus of necrosis is of rather recent origin.

As a rule, necrosis of bone marrow is never so rapid that a sequestrum forms without some traces of reaction. Therefore, although a necrotic area may appear to be of equal density throughout, the bony trabeculae very close to the zone of tuberculous granulations usually show definite lacunar outline, although included in caseous material. This indicates that the subchondral infection extended into the epiphysis for a short time, at any rate, before necrosis of the whole area occurred. This is in contradistinction to the infarct type of necrosis where death of involved tissue occurs simultaneously.

Interpretation of Necrotic Tissue.—The chief difficulty of interpreting changes in tuberculous, or suppurative, necrosis of bone marrow is that disintegration of structures makes it impossible to determine what type of tissue underwent necrosis. In aseptic necrosis it is usually quite easy to make out the histologic structure, so that tissual classification can be made despite lack of nuclei. Such recognition in caseated bone marrow is almost impossible, because decay and disintegration of tissue into an amorphous material apparently occurs so rapidly that the structure affected loses its histologic characteristics almost immediately. Thus, it is quite possible that sudden caseation of fatty bone marrow may present, in a very short time, the same picture as disintegration of tuberculous granulation tissue, cellular bone marrow or even fibrous bone marrow.

The presence of fat holes in caseous material is not always an indication of origin from fatty bone marrow, because similar fat holes can also be found in caseated lymph nodes, where the preexisting amount of fat is certainly inconsiderable. The fat holes may be due to the content of degenerated fatty substances in caseated material. In certain cases of florid tuberculosis, for example, where a rapidly spreading secondary tuberculous osteomyelitis is present, necrotic bone marrow foci show irregular central fat holes, apparently formed by confluence of necrotic fatty bone marrow cells. Quite typically, the necrotic foci show caseated centers, surrounded by many fat holes and by tuberculous granulations, rather than fatty bone marrow. In that event, the arrangement of the fat holes around the center of necrosis probably is due to the extraction of fatty substances at the periphery of necrotic areas.

The only reliable landmark, as is often the case in bone pathology, lies in the bony trabeculae, whose outlines and density offer interpretative data. The different stages of osteoporosis, and especially osteoclasis, often furnish a rather detailed explanation of necrosis of bone tissue in various periods. These changes have already been considered. However, all bone resorption is not a simple osteoclastic process. While it is quite true that the bony trabeculae are frequently lacunar in outline, they may nevertheless be smooth and thin. At the endosteal surface mononuclear cells can be seen; in some instances, these cells are certainly capable of bone resorption.

An interesting finding is the presence of osteoid layers on trabeculae

included in tuberculous granulations. The borderline between calcified and noncalcified bone tissue is sometimes sharply lacunar; quite often, however, there is gradual fading from calcified to noncalcified tissue. The significance of these osteoid layers is still doubtful, but their appearance in connection with rapid bone resorption suggests halisteresis supplementing cellular bone resorption. On the other hand, it is also possible that the continuous process of bone apposition, as it occurs throughout life, may become altered by an inflammatory process, which causes local changes in tissue chemistry, most likely affecting the p_H. This alteration may be sufficient to account for the formation of osteoid tissue.

Fate of Sequestra.—Following necrosis of the dissecting tuberculous gran-

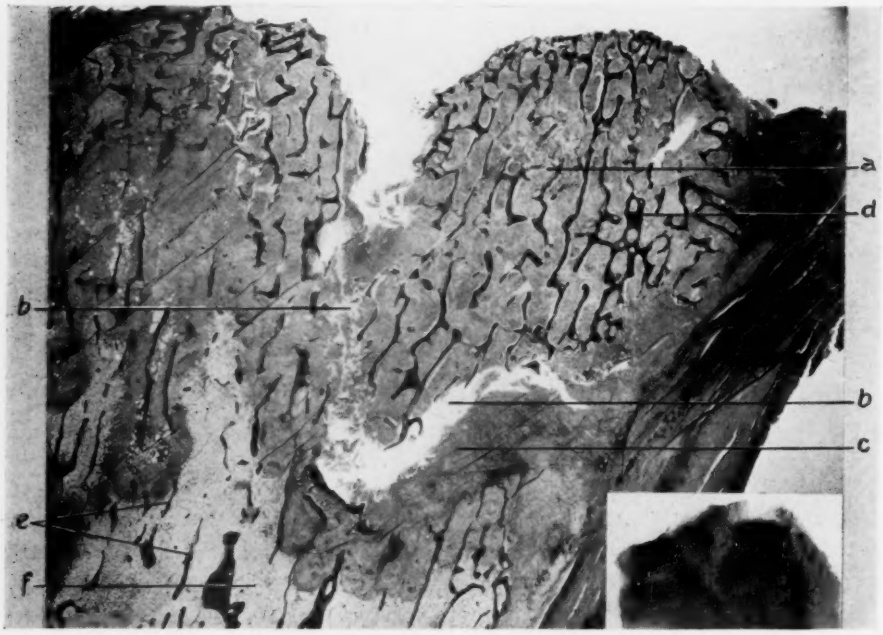

FIG. 24.—Trauma may effect the separation of a necrotic focus *a* so that the zone of separation *b* represents an intra-articular fracture space, as yet unattended by reaction in the adjacent necrotic tissue *c*. The sclerosis of the necrotic trabeculae *d* stands out in contrast to the porotic living trabeculae *e* in fatty bone marrow *f*. The inset shows the roentgenologic appearance of the sequestrum.

ulation tissue, further changes in the sequestrum itself can occur only by trauma or molecular disintegration. The rôle that trauma plays in breaking off portions of the articular surface has already been mentioned. Smaller fragments of spongy bone are very frequently found on the joint surface in the more advanced stages of tuberculous arthritis, and it is quite possible at times that even greater parts of the surface may break off. This is especially true in cases where a focus of necrotic sclerotic trabeculae separates from the adjoining porotic bone and protrudes into the joint cavity. This elevation leads to more irritation of the focus due to motion which is especially marked at the zone where sclerotic bone meets porotic bone. The motion leads to decomposition of bony trabeculae into smaller fragments,

exclusive of osteoclastic resorption by tuberculous granulations. The marrow spaces along this zone contain many small irregular pieces of calcified material, evidently fragmented trabeculae. Thus, trauma appears to be as important a factor in the separation of tuberculous sequestra as the active process of dissection (Fig. 24).

If considerable portions of the subchondral bone are lost by erosion, the

FIG. 25.—The large triangular defect in the subchondral bone *a*, filled by necrotic débris *b* and small bony fragments *c*, represents the area previously occupied by a sequestrum, which probably has been extruded into the joint cavity *d*. The extreme porosis of the surrounding bone tissue is marked. The inset illustrates the roentgenologic appearance of the bony defect.

sequestrum, instead of protruding into the joint cavity, may lie in a depression of the joint surface. In part, this may be due to a relative increase in the size of the bony defect by removal of bony fragments through resorption by tuberculous granulations. On the other hand, the sequestra may be completely extruded into the joint cavity, leaving a triangular defect in the

joint end, which is surrounded by porotic bone tissue and filled by caseated material containing a few bony trabeculae with lacunar outline and markedly decomposed joint cartilage (Fig. 25). This would indicate that the sequestrum is partly resorbed, partly extruded into the joint, where it becomes further disintegrated.

Healing of a tuberculous sequestrum, even of considerable size, is possible by encapsulation (Fig. 26). Dissection of a necrotic area from the

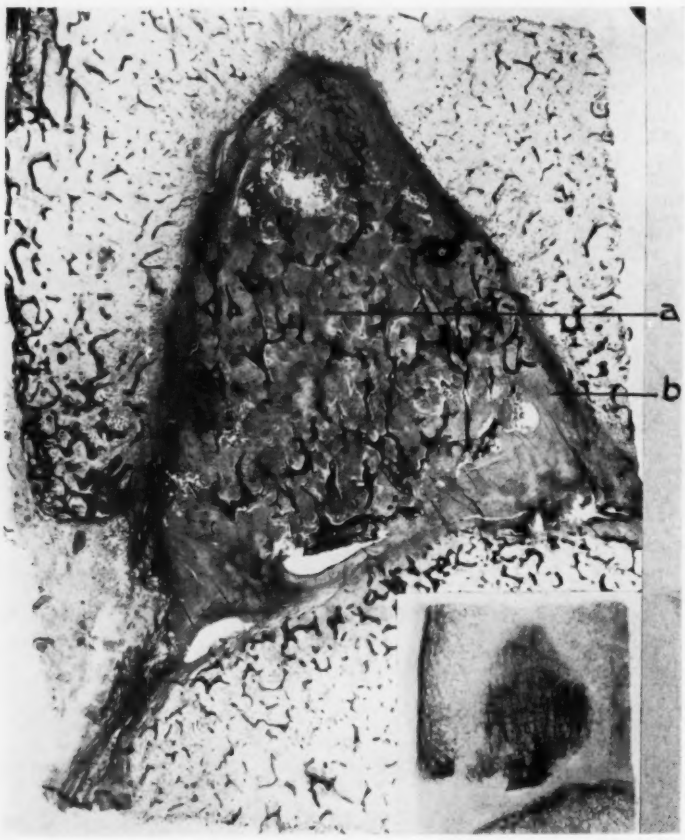

FIG. 26.—A sequestrum *a* of the lower end of the tibia has been partially extruded into the tibio-astragaloid joint. The sequestrum subsequently became encapsulated by a dense fibrous tissue wall *b*, after which all activity within the sequestrum ceased. Again, marked contrast is noted between the sclerotic necrotic bone and the porotic living bone which surrounds it. The inset shows the roentgenologic appearance of this sequestrum.

surrounding tissue may be completed by tuberculous granulations, which undergo fibrous condensation with the formation of a dense capsule. This fibrous wall around the necrotic area buries the focus and prevents further resorption. This phenomenon is well known from studies of tuberculosis in vertebral bodies, where necrotic areas may remain encapsulated throughout life. The lacunar outlines of the trabeculae in the sequestra do not indicate activity, but may be attributed to resorptive changes which occurred in an

earlier period, when the tuberculous granulations were still present. However, if only a few tubercles are present, there is still a possibility of a flare up of the infectious process, augmented by traumatic irritation or lowered general resistance.

SUMMARY.—The subchondral wedge-shaped area of necrosis, resembling a sequestrum is often a diagnostic feature in joint tuberculosis. Unlike the sequestrum in nonspecific osteomyelitis, it need not be dissected free from its surroundings, but may merely represent a subchondral area of necrosis which appears denser in the roentgenogram. The bone infection is usually secondary to an extensive joint involvement; invasion frequently occurs at the joint margins, where the cartilage is thin and the cortex is protected by a delicate synovia only. The advancing zone of infection is demarcated by tuberculous granulations, which may undermine the joint cartilage and even cause it to desquamate in its entire thickness.

Primary bone infection occurred in only 20 per cent of the joints studied microscopically. The infarct type of wedge necrosis of bone, due to vascular occlusion, occurs only rarely. Foci of hypertrophic arthritis, devoid of protective joint cartilage, are often selected as sites of tuberculous invasion contrary to the opinion that hypertrophic arthritis is a protection against tuberculosis.

An area which has undergone tuberculous necrosis becomes inactive as soon as the bone marrow dies. The bony trabeculae therefore remain sclerotic, whereas the surrounding living bone tissue undergoes resorption and becomes porotic. The sequestrum can now become changed only by trauma or molecular disintegration. Trauma may cause portions of the joint end to be broken off. It may then protrude into the joint cavity where it is ground into tiny fragments, or it may be extruded to the exterior if the joint cavity connects with a sinus tract. On the other hand, the sequestrum may become encapsulated in fibrous tissue and remain unchanged indefinitely.

Interpretation of necrotic tissue is difficult, because disintegration makes tissual classification impossible. Often the bony trabeculae furnish the only reliable landmarks, which offer clues as to the preceding course of tissue changes.

The pathologic material was obtained from the private collection of Dr. Ernst Freund, to whom I am indebted for invaluable aid in preparing this paper.

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THE SURGICAL TREATMENT OF HUMAN BITES

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ABOUT three and one-half years ago an investigation of the treatment of human bites was begun at the Beekman Street Hospital, New York City. A search through the records of that institution revealed that the most diverse methods of treatment had been followed, and a discussion of the problem at staff conference brought out that there was not even unanimity of opinion as to just what ought to be done. The writer undertook to investigate the problem and attempt to work out a satisfactory routine treatment which could be followed throughout the hospital.

Any surgeon who has seen some of the results in these cases will appreciate the seriousness of the problem. Apparently the human is the dirtiest of all mouths. In the frankly infected bite there is a foul discharge and a creeping phlegmonous process which frequently extends rapidly up the arm despite the sometimes heroic measures adopted to check it. The organisms involved are usually described as anaerobic streptococci along with spirilla and fusiform bacilli of the Vincent group. The writer has personally seen two deaths from such infections.

Undoubtedly in a fresh case the safest procedure would be actual cauterization or a radical débridement with complete excision of all contaminated tissues. However, these are both formidable procedures and in the hand where most of these injuries occur would involve the sacrifice of important structures. For such procedures hospital admission and extensive local or even general anesthesia would be required. Moreover, permission to perform them would undoubtedly be refused by a considerable number of patients. It was necessary to select some method of treatment that could be applied rapidly by an intern in the emergency room or even, when necessary, on ambulance calls. For many years chemical cauterization has been used for dog bites and as can be judged from our own experience and the reports of others, the results have been good. It was, therefore, determined to use this method in all cases of human bites over a period of time and then attempt to evaluate the efficacy of the treatment.

During the period of 30 months between July 8, 1932, and December 31, 1934, a total of 122 human bites were treated. For the first half of this period all cases were reported immediately to the writer, and all were either seen by him at once or their treatment was directed by him to the house surgeon. An attempt was made to have all cases kept under his personal care during their entire treatment thereafter. All wounds were freely swabbed out with fuming nitric acid on a cotton applicator and immediately flushed with cold water. There is no doubt that this is a

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painful procedure, but the pain is evanescent. Wet dressings were applied in all cases. No wounds were sutured. Since bacillus tetani has never been reported as present in the human mouth and no case of tetanus has, to the best of our knowledge, followed a human bite, no tetanus antitoxin was given. The nitric acid was applied even where joints had been opened and tendons exposed. No anesthesia, local or general, was used. During the latter half of the period in question the writer's routine was applied but he did not personally take charge of all cases. There was no difference in the results in the two groups, and all figures represent the total for the two series.

In the 122 cases cared for in this period bites of all parts of the body were represented but in by far the largest number the fingers and hands were involved. Bites of the fingers were the most frequent—53. Injuries to the hand were only slightly less in number—40 (Table I). This latter group was largely made up of cases in which the injury was not, strictly speaking, a bite, almost all having been produced by striking someone in the mouth and injuring the hand on the teeth. In general the injuries in this group were deep and in many cases the metacarpophalangeal joints were involved, the tooth penetrating directly into the joint. Two of the three poor results in this series belong in this group. Ten bites involved the face and head, and 19 various other parts of the body. The majority occurred in adult males.

TABLE I

DISTRIBUTION OF INJURIES

Total Cases	Fingers	Hands	Faces and Heads	Other Parts
122	53	40	10	19
	43%	33%	8%	16%

For purposes of analysis the entire series of 122 cases may be conveniently divided into three groups. Group one consists of 41 cases in which treatment was carried to completion or nearly so. The time under treatment varied from 2 to 100 days. Excluding the three poor results, from 2 to 31 days, an average of about 12 days. The results in 38 cases were described as "good." By this was meant that no serious infection developed and that the function of the part was not obviously impaired. Scarring was not extensive and was not taken into consideration in evaluating the results. Of the three poor results one was described as "fair," one as "bad," and one as "poor." The first of these cases did not come to the hospital until one month after his injury so we do not feel responsible for this failure and it will be dropped in the statistical summary. One of the metacarpophalangeal joints was involved with an eventual loss of about 50 per cent of the normal motion. The second case was seen five hours after injury and the routine treatment applied. Extensive infection developed and admission to the hospital was necessary. An abscess developed on the dorsum of the hand, which was opened with the actual cautery. Following this procedure which we now believe was unwise, the infection progressed rapidly, and it was necessary to hospitalize him for

30 days. The metacarpophalangeal joint of the index finger was obviously involved and was widely opened. All wounds were finally healed 38 days after the injury. He received physiotherapy for 62 more days but motion in the joint was completely lost. The third case in which the result was noted as "poor" came to the hospital 24 hours after the accident but the first examiner stated that in his opinion the wound was several days old. Involvement of a joint of the finger occurred and this patient was under treatment for 43 days. About 70 per cent of the motion in the joint was permanently lost.

The second group of 63 cases comprises those who made only one visit to the hospital. Of these 48 must be dropped from statistical consideration. For the most part they were from the floating population of New York's lower East Side waterfront and it was found impractical to check on their final results. In the remaining 15 patients we were able to determine the course and the outcome. All can be classed as good results.

The third group comprises 18 cases which were seen more than once but were not in general under treatment long enough to warrant more than an estimate of the result. Of these nine were apparently on the way to recovery. It would be unwise to hazard even a conjecture about the remaining nine.

Our statistical summary must then be built primarily on the 40 cases treated from beginning to healing and on the 15 which were seen only once but in which we were able to find out the end-result. In these two groups there were 55 cases. The results can be called satisfactory in 53 cases or 96 per cent and unsatisfactory in 2 cases or 4 per cent. In addition we have the nine cases which we were fairly sure were on their way to recovery. Adding these we have a total of 64 cases with 62 good results, or 97 per cent and 2 bad results, or 3 per cent (Table II). Considering some of our previous unfortunate experiences with these cases we have been definitely encouraged by these results. We do not regard the problem as solved but we feel that a definite advance has been made in handling this simple but serious type of injury.

TABLE II

SUMMARY OF RESULTS OF TREATMENT

Cases Followed Sufficiently to Know Results	Good Results	Cases Followed Sufficiently to Estimate Results	Good Results	Cases Lost
55 *	53 96%	64 *	62 97%	57

* One case omitted from summary.

We feel that cauterization with nitric acid should be done even in cases of several days' standing. In addition to the one questionable 24 hour case which did badly, several appeared in our series first seen from one to four days after injury. All were cauterized and, with the exception of the one case noted, all did well. We have not found the after effects of the nitric acid burns particularly painful. In the average case the wound drains for

about five or six days, but, and this is important to note, the drainage does not have the foul odor so characteristic of infected human bites. Wet dressings are maintained during this period. By about the sixth day the eschar has dissolved or separated and most of the wounds heal cleanly from the bottom. Most cases are discharged in two weeks or less. The nitric acid eschar rarely seems to cause retention of secretions. This probably occurred in our unsatisfactory cases.

The following instructions are posted in the Emergency Room for the guidance of the intern staff:

(1) All human bites are to be thoroughly wiped out with fuming nitric acid. The acid is to be applied with a cotton wound applicator of a size appropriate to the wound and the cotton is to be saturated but not dripping. If any nitric acid is spilled on the skin the area must be immediately washed with cold water.

(2) Wet dressings are to be applied in all cases and instructions given for hot soaks at home.

(3) All cases of human bites are to be referred to the out-patient department to be seen the following day.

(4) No tetanus antitoxin is to be given.

(5) No wounds of this type are to be sutured.

Cauterization with nitric acid may seem a brutal procedure, but it is only necessary to see one of these creeping infections start up the arm to realize that heroic measures are fully justified if they will prevent such an outcome.

BRIEF COMMUNICATIONS AND CASE REPORTS

HEMANGIOSARCOMA OF THE MEDIASTINUM*

HOWARD LILIENTHAL, M.D.
NEW YORK

THE history of the patient herewith presented was detailed in the ANNALS OF SURGERY, **85**, 615–618, April, 1927, in the Proceedings of the New York Surgical Society for December 8, 1926, when the case was first reported.

Abridged Résumé.—Phyllis H., female, at the age of two years became paraplegic. A diagnosis had been made, at the Hospital for Joint Diseases, by Dr. Alfred W. Pollak, of an enormous mediastinal tumor involving more than two-thirds of the thoracic space, which had eroded the ribs at one point, and was obviously causing the paraplegia from pressure upon the cord.

A small, posterior mediastinotomy was performed April 15, 1924, and a generous piece of the tumor removed for examination, the pathology of which was diagnosed as angiosarcoma by Dr. F. S. Mandlebaum. The wound healed nicely, and treatment with Coley's mixed toxins was immediately begun by Doctor Pollak, beginning with one-twenty-fifth minim. A number of injections were made which caused very severe reactions, but, only three weeks after the operation, the child began to walk, the relief apparently having resulted from the decompression. This improvement continued, and a series of roentgenograms by Dr. H. B. Philips demonstrated the gradual disappearance of the tumor mass, and in October, 1926, a roentgenogram by Doctor Jaches revealed a normal chest. The child has been well ever since.

Doctor Gross, Director of the Laboratory at Mount Sinai Hospital, diagnosed the tumor as a hemangio-endothelioma. Dr. James Ewing stated that it was a "Malignant cellular tumor of embryo type, composed of many blood sinuses, lined by two or more rows of tumor cells. Very delicate stroma." It was his opinion that the tumor was extremely malignant.

The patient is now an apparently normal child of 14 years. Roentgenograms have been made every year, and show no abnormality.

Here, at any rate, is a case in which there is no difference of opinion between the pathologists. From the clinical side it certainly was one which offered an extremely grave prognosis.

Doctor Lilienthal stated that he was one of the few who had persisted in the administration of Coley's toxins in inoperable cases, and also as a prophylactic measure following operation. From an experience with some dozen cases, he felt more and more convinced that in the absence of any

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other form of treatment which even remotely promised results, the toxins should be employed as a matter of course.

Discussion. Dr. Bradley L. Coley (New York) thought that Doctor Lilienthal had had an unusually favorable experience with the toxins, his continued interest throughout the years having been rewarded more fully than that of most others who have used toxins in a considerable number of cases. The unfortunate feature of this treatment is the uncertainty of obtaining favorable results. One may employ the toxins in several cases without seeing any improvement, which is especially apparent when one treats a large number of patients. Moreover, the combined use of the toxins with other methods of treatment always leaves open the question, when the patient remains well, as to what was responsible for the favorable result. Was it due to operation, radiation, or toxins?

In general, one hesitates to extol any one method when others, also, are of value, and Doctor Coley said he would be the last to advocate the use of toxins alone where either surgery or radiation, or both, might be helpful. However, in the aggregate, a considerable number of cases in which toxins only have been used, proved by microscopic examination to be malignant, following treatment by toxins the patients have survived an appreciable time, upwards of five or even ten years. The mediastinal case presented by Doctor Lilienthal is one that fulfills those requirements. There was no irradiation. The clinical and microscopic diagnosis leaves no doubt as to the malignancy of the process.

Doctor Coley regretted that Dr. Wm. B. Coley could not be present to show one of the most dramatic cases ever encountered. That patient was treated not by him, but by Drs. S. L. Christian and L. A. Palmer of Staten Island. It is known as the "Marine Hospital Case."[1] The patient had an endothelial myeloma of the tibia. An amputation was performed. There was an obvious recurrence in the amputation stump. The patient then developed numerous metastases in various other locations. He received tremendous doses of toxins, but no irradiation at any time. He is well and was shown last January before the American Academy of Orthopedic Surgeons. He is registered as an endothelial myeloma by the Bone Sarcoma Registry (Reg. No. 1143).

There were a number of recorded cases comparable to that of Doctor Lilienthal, and he believed that this should encourage one to anticipate, at least, an occasional similar result in others, and that we should use the toxins in conjunction with whatever other methods, including irradiation and surgery, are applicable to the individual case.

In May, 1934, Dr. Bowman C. Crowell, Registrar of the Bone Sarcoma Registry of the American College of Surgeons, presented the five year survivals of primary malignant bone tumor cases. At that time there were only nine endothelial myeloma cases that had passed the five year mark, and six of the nine had been given toxins in conjunction with other forms of treatment. There are no cases, microscopically confirmed, in which irradiation alone has produced a five year cure.

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JAUNDICE DUE TO OBSTRUCTION BY AN ABERRANT VESSEL AND ADHESIONS *

RUSSEL H. PATTERSON, M.D.

NEW YORK

Case 1.—A single woman, age 26, was admitted to Ward M-4, Bellevue Hospital, Second Surgical Division, October 22, 1933. Since infancy she had been subject to "bilious attacks," and always seemed to have had a very sensitive stomach and digestion.

During the two years before admission, she had experienced intermittent attacks of pain in the right upper quadrant, often associated with jaundice. Although neither the pain nor the jaundice was severe, both were very annoying, and the jaundice was particularly in evidence on several occasions when examined. She had had no chills or fever; no diarrhea or clay colored stools. The findings in a gastro-intestinal and gallbladder roentgenologic series were negative. Duodenal drainage was also negative, in that it failed to yield any B bile.

The patient entered the hospital for operation during a symptom free period. Examination revealed a young woman, normal in every respect. Blood pressure 122/68.

Operation.—October 23, 1933. Under gas-oxygen anesthesia, a right rectus muscle splitting incision was made. The gastrohepatic omentum was very short, puckering up, as it were, the common duct, the portal vein and the hepatic artery therein contained; and also bringing the pylorus and the first portion of the duodenum much closer to the gallbladder and liver than is usual. Furthermore, there was a fibrous band containing an artery which arose or came off of the superior aspect of the first portion of the duodenum. This artery was probably a branch of the gastroduodenal artery. The artery and the fibrous band were wrapped around the anterior, right lateral and posterior aspects of the lower third of the common duct in such a way as to rotate or twist and constrict the duct until the duct, at that point, was not more than one-quarter or one-fifth of its normal diameter.† The common duct was not noticeably thickened.

Procedure.—The peritoneum covering the gastrohepatic omentum was divided transversely and the common duct, hepatic artery and portal vein straightened out considerably, but the common duct remained constricted until the artery and the fibrous band wrapped around it were divided. The duct then returned nearly to its normal diameter and, upon compressing the gallbladder, it emptied easily. Believing that this aberrant vessel and fibrous band caused the intermittent biliary obstruction, nothing further was done and the abdomen was closed without drainage. The postoperative course was entirely uneventful, and when examined January 8, 1936, two years and two months postoperative, there had been no return of her jaundice.

Case 2.—Mrs. H. S., age 47, was admitted to Ward M-5, Bellevue Hospital, Second Surgical Division, July 15, 1935. For more than one year she had suffered occasionally from nausea with regurgitation of bitter material, and chronic constipation, aggravated by coffee and fatty foods. Six months before admission she was confined to bed for one month because of jaundice and pain in the right upper quadrant, which radiated to her right shoulder. During the past month she had vomited several times. One week before admission, the discomfort in the right upper quadrant increased markedly and jaundice appeared.

Physical Examination.—An apparently healthy, though definitely jaundiced, very obese woman. Temperature 100.4° F., pulse 78, respirations 20, blood pressure 120/80. There was moderate tenderness in the right upper quadrant and the urine showed three plus bile.

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† The gallbladder was normal but was three-quarters filled with bile. It would not empty when compressed.

Laboratory Data.—van den Bergh Test—Direct: Delayed; Indirect: Slightly positive. N.P.N. 34. Blood sugar 78. Blood type, Group I. W.B.C. 8,500. Icteric index 5. Urine showed bile three plus. Stools brown.

The gallbladder could not be visualized roentgenologically after administration of the dye, suggesting pathology.

Within 23 days, the patient's jaundice cleared up entirely and she was free of abdominal tenderness and symptoms of every kind. However, in view of the fact that she had been so definitely jaundiced six months before and again at the time of admission, it was thought advisable to explore the common duct.

Operation.—August 7, 1935. Under gas-oxygen anesthesia, a right rectus muscle splitting incision was made. The gallbladder, greatly thickened, contained many faceted stones. The cystic duct was stenosed. The ampulla of the gallbladder was greatly thickened. The common duct was enlarged, thickened and adherent to the ampulla of the gallbladder in such a way that the common duct was bent upon itself, so that there was complete, or practically complete, obstruction of the lumen. There were fairly dense adhesions involving the gallbladder, common duct, gastrohepatic omentum, pyloric end of the stomach, duodenum and the hepatic colon.

Procedure.—All adhesions were separated. The common duct was separated from the ampulla of the gallbladder with considerable difficulty, but this did not correct the angulation in it. The gallbladder was removed. The common duct was opened, thoroughly explored, but no stones found. The bile was muddy. Even after freeing the surrounding adhesions we were unable to straighten out the common duct. A large T tube was passed down through the angulation in order to hold the common duct straight and prevent its bending upon itself. A cigarette drain was placed down to Morrison's pouch and the wound was closed.

The postoperative course was uneventful. The T tube was removed on the nineteenth postoperative day. The patient has reported at intervals, and informs us that she has had no further jaundice or symptoms.

COMMENT.—Two cases are reported. In one there were congenital anomalies including an aberrant vessel, and in the other the jaundice was due to adhesions obstructing the duct.

The first case was unusual in that the obstruction was due to the anatomic variation, there being a shortened gastrohepatic omentum and an anomaly of the blood vessels with a band of tissue similar to other bands described as occurring about various portions of the gastro-intestinal tract. The constriction of the common duct was unquestionably the cause of the jaundice, as at the time of operation it was impossible to empty the gallbladder compression before the aberrant vessel was divided. However, after this was severed the gallbladder could be emptied easily.

Dr. William E. Ladd of Boston recently published an article[1] in which he reported 45 cases of "Congenital Obstruction of the Bile Ducts," and divided them into seven groups. The first case herewith presented does not fit into any of these groups, because it demonstrated extrabiliary variations constricting the common duct, whereas Doctor Ladd specifically referred to anatomic variations of the bile ducts.

In the second case, the jaundice was apparently due to an angulation of the common duct with almost complete obstruction. Although jaundice in postoperative cases due to adhesions, scar tissue or other complications, does occur, jaundice caused by the conditions found in this instance is unusual.

Dr. Ellsworth Eliot, Jr.,[2] has reported three cases similar to this second case, but in his series the obstruction was due to inflammation resulting from a duodenal ulcer.

Either of the cases that have been presented might have had a small stone, mud or sand in the common duct which could have caused jaundice owing to constriction of the common duct, even though so small an amount of mud or a very small stone would not necessarily have caused jaundice in a common duct with a normal lumen.

The intense pain that is commonly a feature of intermittent jaundice due to common duct stone was not a prominent symptom in either of the cases presented. Although diet played no rôle in the first case, the second patient did experience symptoms following the ingestion of certain articles of food, but it must be remembered that she had a definitely diseased gallbladder. Rest in bed afforded the inflammation an opportunity to subside by eliminating the downward pull of the liver on the angulated common duct.

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Discussion.—Dr. Guilford S. Dudley (New York) confessed that personally he had never seen a case with similar, comparable cause of obstruction to the common bile duct, and found it a little difficult to understand why the patient should have had recurring attacks of pain, without progressive jaundice, if the obstruction to the common duct had been due to an abnormal anatomic band. A calculus in the common duct could have been the cause of jaundice, in either patient.

Calculi in the gallbladder may cause no symptoms, and there may also be "silent calculi" in the common duct. A case in point, operated upon January 7, 1936, by the speaker, was cited. The patient gave no history of jaundice, but not only was there a calculus in the gallbladder, but in the common duct as well, which, although apparently normal on inspection, revealed two small calculi on palpation, and when opened it was found to contain five small calculi. There may even have been more that were not detected.

He cited another case with a history of having been operated upon in 1918, a cholecystectomy having been performed. In 1919 she was again operated upon for recurrence of symptoms due to common duct stones, which were said to have been removed at this time. She remained symptom free until 1927, when she had an attack of jaundice which subsided spontaneously. There were no further symptoms until 1932, when she suffered a series of attacks of pain associated with jaundice. Her icteric index was 9. She was operated upon with a diagnosis of common duct stone. Doctor Dudley presented the stone found in her common duct, calling attention to the very interesting fact that the branching of the stone represented the two hepatic ducts. Since the last operation, January, 1933, the patient has remained well.

Dr. Joshua E. Sweet (New York) interpreted the obstruction of the duct from an aberrant vessel as an unusual instance of what is a normal process in the development of the gallbladder and its ducts. The cystic artery grows out and adheres to the gallbladder at an early stage, before the gallbladder and ducts have reached their final development. When the gallbladder

and ducts develop, there is no room for the duct to develop in a straight line, and thus it is drawn into an S-shaped kink. An accentuation of this process apparently developed in Doctor Patterson's first case.

The second case presented by Doctor Patterson, he thought, represented a situation much more common than suspected. The patient had had an attack six months before she was examined, and had been in bed for one month at that time. That attack probably represented an attempt by the gallbladder to extrude stones, during which attempt the gallbladder very commonly becomes adherent to adjacent viscera, most frequently to some portion of the intestine. As a rule, the stones pass and the adhesions usually separate. But sometimes they do not. This would explain why this woman was fairly comfortable when lying down, *i.e.*, when in the position in which the adhesions had formed, but experienced more difficulty in an erect posture.

Referring to the stone shown by Doctor Dudley, he thought that common duct stones of that type, that is, those which occur in the common duct when there are no stones found in the gallbladder, are very characteristic in their color and also in the fact that, on drying, they fracture by radial cracks and disintegrate completely. The portion of the stone missing in the specimen shown was broken off from a branch which apparently had extended into the stump of the cystic duct. This missing portion Doctor Sweet had left unvarnished in order to see whether it belonged in this category, and it did disintegrate. The larger portion was varnished for preservation. These stones occur frequently in the Chinese, and he surmised that they were the result of a mixture of pancreatic juice and bile in the common duct. He also emphasized that these cases demonstate a fact, well understood, but often forgotten; namely, that jaundice is a symptom of common duct pathology and has no relation whatever to gallbladder disease.

THE TREATMENT OF INFECTIONS OF THE FACE BY PROPHYLACTIC VENOUS OBSTRUCTION

CLYDE A. ROEDER, M.D.

OMAHA, NEB.

INFECTIONS of the upper lip, cheeks, lateral surfaces of the nose and forehead are so frequently followed by involvement of the adjacent veins and an extension into the cavernous sinus, that the original lesion cannot be given too much consideration. This central portion of the face is drained by a most interesting circle of venous blood, which, in sequence, and starting from the upper lip, consists of the upper facial vein, the angular, the transorbitals (superior and inferior ophthalmics), the cavernous sinus, the vein connecting the lower transorbital (inferior ophthalmic) with the pterygoid plexus, the pterygoid plexus, and the venous connection between the pterygoid plexus and the facial vein. This is very well illustrated by Figures 1 and 2.[6]

These venous channels are evidently without valves, and the blood may flow in either direction; depending upon an obstruction or greater pressure existing in the internal or external portion of the circle. If the internal portion in the region of the pterygoid plexus were obstructed, the blood would flow from the cavernous sinus toward the heart through the transorbital,

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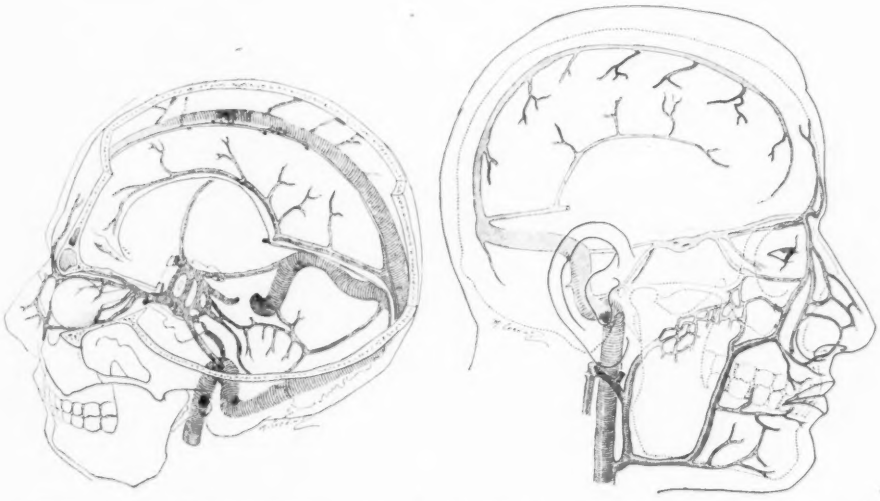
angular, and facial veins. If the obstruction existed in the orbital or facial (external) portion of this venous circle, the blood from the cavernous sinus would flow toward the heart through the pterygoid plexus. The physics of these two obstructions should be kept in mind, particularly when confronted by a possible invasion of the facial veins from infection of the upper lip, cheeks, forehead, or lateral surface of the nose.

No one can state when these venous channels will become involved; nor after involvement does take place, whether or not the cavernous sinus will



FIGS. 1 and 2.—Note anastomosis at upper inner angle of eye between superficial vessels and the superior ophthalmic vein, and the connection between the deep pterygoid vessels and inferior ophthalmic vein. None of these veins have valves. (Coller, F. A., and Yglesias, L. Surg., Gyn. and Obst., 277, February 15, 1935.)

become infected. Since it is well known that septic cavernous sinusitis is a fatal complication, any method for its possible prevention is worthy of consideration. Prophylactic ligations of the angular veins have been practiced [1,2,3,4,5,6] with not unfavorable results. We are all aware, I feel sure, that recovery may occur without a ligation of the angular vein. But a more serious question arises in those cases which developed a cavernous sinusitis, *i.e.*, would this fatal complication have occurred if the angular and transorbital veins had been artificially obstructed early in the course of the infection? Transmission of an infection to the cavernous sinus through the pterygoid plexus is a possibility, but more remote than through the angular vein, particularly when the latter is obstructed and the blood pressure in the former is thereby increased. Venous obstruction is worthy of consideration if it can be applied prophylactically, and particularly with no risk, no deformity, and very little discomfort to the patient. With this portion of the above described venous circle artificially obstructed, an infection through the angular and transorbital veins is prevented and coincidentally there results an increase in the venous pressure in the pterygoid plexus. A septicemia

may result with or without any form of venous obstruction, but a cavernous sinusitis may be prevented by external prophylactic venous obstruction.

In 1931 I constructed an apparatus (Fig. 3) which any physician or surgeon can apply during the early stages of infections of the upper lip and adjacent regions. The advantage of this apparatus over ligation of the angular vein is that no operation is necessary to obstruct this vein, and that it also obstructs one of the transorbital or inferior ophthalmic veins which may transmit septic emboli even after the angular vein has been ligated.

It was used once on a patient in December, 1931, and was worn with no discomfort and with a successful outcome. During the surgical drainage

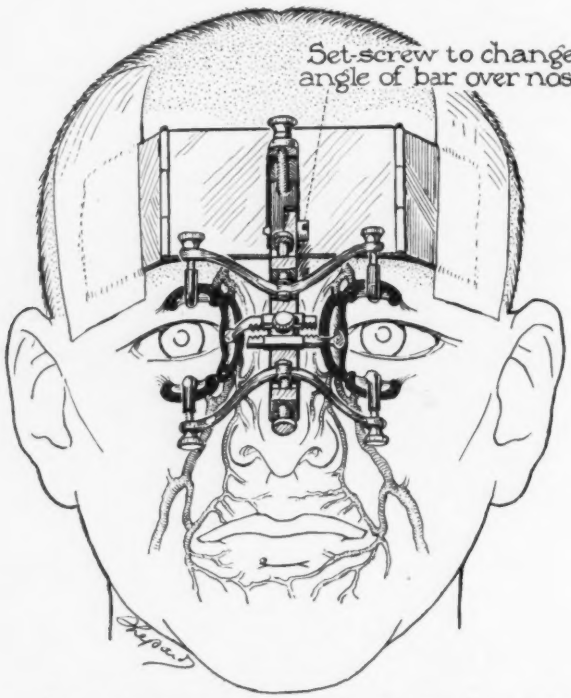


FIG. 3.—Apparatus in place. Note that all veins entering orbit are obstructed. The head band might be longer and lined with sponge rubber in order to increase immobilization by a firmer bandage without much pressure discomfort.

of the upper lip, it was left in place in order to block emboli from extending upward. How long to leave this apparatus in situ after infections of the face have originated I do not know; but certainly if it is to be used, it cannot be applied too soon.

It is offered merely as a simple method of obstructing the angular and transorbital veins during deep and suspiciously dangerous infections of the face, adjacent to the above described veins. The apparatus should be further refined, particularly as to its immobility. An adjustable band completely encircling the head might be an improvement. The venous compression plates and the bar over the nose are lined with sponge rubber, and during their

application the patient's eyelids should be tightly closed. I am well aware of the fact that my one case offers nothing more than a suggestion, and that the subject is still open for discussion as to whether or not early venous obstruction is a worth while procedure in addition to the more essential and proper treatment, operative or nonoperative, of the primary lesion.

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GUMMATOUS INFILTRATION IN MUSCLE

REPORT OF TWO CASES

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CHICAGO, ILL.

THE two cases of gummata occurring in muscle, reported herewith, came under our observation at Cook County Hospital within several weeks. The possibility of diagnostic error and the paucity of reported cases prompted this presentation.

Kaufmann[1] states that syphilis of muscle occurs in two forms; one, a chronic cicatrizing thickening of muscle connective tissue, which leads to atrophy of muscle parenchyma (syphilitic fibrous myositis) and usually involves the biceps and occasionally the masseter muscles, and often leads to contractures. The second type occurs in the form of a gumma which spreads into the neighborhood of muscle, and appears as a protruding, immobile tumor with a tendency to destruction. Adami and Nicholls[2] state that these tumors must be differentiated from sarcoma. Jordan et al.[3] describe eight cases of gummatous infiltration into muscle, and Milch and Galland[4] report five instances, terming them pseudoneoplastic leutic granulomata, and stress the difficulty of differentiating these tumors from malignant growths.

Case 1.—H. K., white male, 54 years old, was admitted to the outpatient department of Cook County Hospital, complaining of pain in the left forearm, with radiation to the shoulder and wrist. Prior to admission he had been treated at another clinic where sedatives and local hot fomentations were advised. The mass, according to the patient, started spontaneously six weeks prior to admission as a small lump in the center of the forearm and gradually progressed until it involved almost the entire length of the forearm. No previous history of illness was disclosed, and the patient

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emphatically denied syphilis or gonorrhea. In an automobile accident 14 years ago, the patient's left wrist was injured, but he recovered without disability.

The patient has four children living and well. He is a moderate diabetic, controlled on a diet of C-160, P-86, and F-84. Insulin therapy, in the quantity of 20-10-10 units, has been necessary.

On physical examination the heart and lungs were negative. The pupils reacted sluggishly to light and accommodation. There were no pathologic reflexes. Adenopathy was moderate. On the anteromedial aspect of the left forearm was a firm, nodular mass involving the area of the belly of the flexor carpi ulnaris muscle. There was no impairment of muscle function. The tumor was tender to touch, and was adherent for about three-quarters of its length to the skin surface. The patient was reported

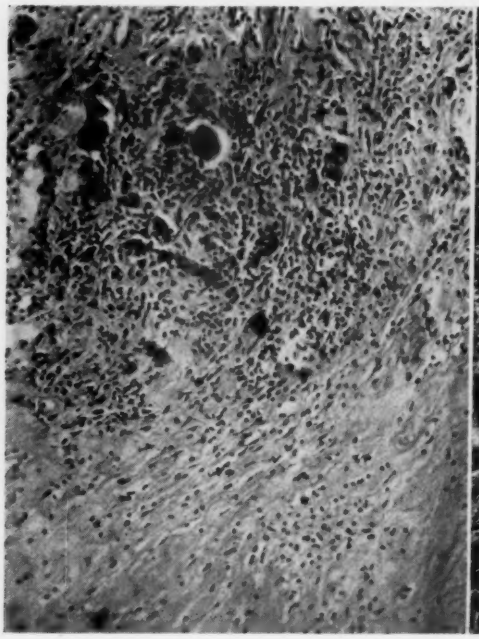

FIG. 1.—(Case 1) H. K. Photomicrograph showing an area of necrosis which is surrounded by an area of granulation tissue with many giant cells. Hemalin-eosin (×170).

FIG. 2.—(Case 1) H. K. Photomicrograph showing an area of necrosis in which bundles of collagenous tissue can still be recognized. At the periphery there is dense connective tissue which is infiltrated by lymphocytes. Van-Giesen (×150).

serologically negative. Roentgenograms of the long bones of the forearm were negative. The age of the patient, the loss of weight, the knobby, adherent character of the tumor and the rapidity of growth suggested a tentative diagnosis of fibrosarcoma of muscle.

Exploratory operation was performed September 29, 1935. Through an elliptical incision the mass was removed in toto, together with the involved skin. The superficial portion of the belly of the flexor carpi ulnaris muscle was sacrificed with the mass, and the deeper, normal appearing portion of the muscle belly was electrocoagulated. A more radical operative procedure was not attempted because the exact nature of the mass could not be ascertained macroscopically, and immediate sections were not available. The wound was closed without tension and two rubber tube drains were inserted, one in either end. These were removed at the end of 24 hours. The wound healed by primary union, except in one small area, which closed at the end of four weeks. The pathologist, Dr. J. Kirschbaum, reported "a specimen containing skin 12.5 by 2 cm., beneath which is a mass 14 by 3.5 by 1.5 cm., and on sectioning is yellow-

tan color and attached to it is a piece of muscle. The tumor shows extensive areas of caseation necrosis and marked perivascular round cell infiltration. The muscle bundles are separated in places by an intercellular accumulation of plasma cells, round cells and single multinucleated giant cells. The histologic picture is that of a gumma" (Figs. 1 and 2). A blood Wassermann later revealed a four plus reaction, and the patient was placed on antiluetic treatment. No impairment of function was noticed at the end of four weeks.

Case 2.—W. A., a colored laborer, 29 years of age, was admitted to the orthopedic outpatient department of Cook County Hospital with the complaint of swelling of the neck of six weeks' duration, associated with pain and local tenderness which had been preceded by a coryza. A feeling of stiffness was present and a gradual en-

FIG. 3.—(Case 2) W. A. Bulging area of involvement has been marked, showing bilateral symmetrical distribution.

largement of the lower part of the neck in the region of the suprasternal notch. The patient had a tickling sensation in his throat but could not cough. Because of the possibility of a granulomatous or malignant tumor he was admitted to the hospital.

Physical examination revealed a bilateral, symmetrical walnut sized swelling in the region of the distal ends of the sternocleidomastoid muscles. There was definite tenderness in this area, and the patient complained of pain on pressure (Fig. 3).

The heart and lungs were negative, and the pupils reacted sluggishly to light and accommodation. The blood Wassermann was reported two plus. Roentgenograms of the involved area were negative. A course of antiluetic treatment consisting of mercury inunctions and potassium iodide was given. One week later the blood Wassermann was negative and the mass was gradually becoming smaller and the tenderness had diminished.

Stimulated by the findings in Case 1, a biopsy was performed and Dr. Kirschbaum gave the following histologic report: "The tissue taken from the sternocleidomastoid muscle shows an extensive necrosis. The smaller sized arteries are thick walled and infiltrated with polymorphonuclear leukocytes. The lumen is frequently obliterated by an organized thrombus. Scattered about are single degenerated muscle fibers with indistinct striations. The histologic picture is that of a gumma."

Dr. L. E. Anderson[5] states that "gummatous infiltration into muscle is a great rarity, but there is nothing distinctive about the process except the extraordinary deforming scar which it may produce."

CONCLUSIONS

(1) Gummatous tumefactions of muscle are uncommon.

(2) These gummata are frequently mistaken for sarcomata.

(3) Wassermann and Kahn tests and a therapeutic test of mercury and iodides should be tried for all suspicious muscle tumors.

(4) They respond well to antiluetic treatment.

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THE AMERICAN BOARD OF INTERNAL MEDICINE (INC.)

THE American Board of Internal Medicine, incorporated February 28, 1936, completed its organization on June 15, 1936. The officers chosen were Walter L. Bierring, M.D., Des Moines, Chairman; Jonathan C. Meakins, M.D., Montreal, Vice-Chairman; and O. H. Perry Pepper, M.D., Philadelphia, Secretary-Treasurer. These officers with the following six members constitute the present membership of the board: David P. Barr, M.D., St. Louis; Reginald Fitz, M.D., Boston; Ernest E. Irons, M.D., Chicago; William S. Middleton, M.D., Madison; John H. Musser, M.D., New Orleans, and G. Gill Richards, M.D., Salt Lake City.

The term of office of each member will be three years, and no member can serve more than two consecutive three-year terms.

The organization of the Board is the result of effective effort on the part of the American College of Physicians in conjunction with the Section on Practice of Medicine of the American Medical Association, and these two organizations are represented in the membership of the Board on a five to four ratio respectively.

The American Board of Internal Medicine had previously received the official approval of the two bodies fostering its organization, as well as that of the Advisory Board for Medical Specialties and the Council on Medical Education and Hospitals of the American Medical Association.

The purpose of the Board will be the certification of specialists in the field of internal medicine, and the establishment of qualifications with the required examination procedure for such certification.

While the Board is at present chiefly concerned with the qualification and procedure for certification in the general field of internal medicine, it is intended to inaugurate immediately after July 1, 1937, similar qualification and procedure for additional certifica-

tion in certain of the more restricted and specialized branches of internal medicine, as gastro-enterology, cardiology, metabolic diseases, tuberculosis, allergic diseases, *etc.* Such special certification will be considered only for candidates who have passed at least the written examination required for certification in general internal medicine. The operation of such a plan will require the active participation and cooperation of recognized representatives from each of such special fields of medicine.

Each applicant for admission to the examination in internal medicine will be required to meet the following standards:

General Qualifications

(1) Satisfactory moral and ethical standing in the profession.

(2) Membership in the American Medical Association or, by courtesy, membership in such Canadian or other medical societies as are recognized for this purpose by the Council on Medical Education and Hospitals of the American Medical Association. Except as here provided, membership in other societies will not be required.

Professional Standing

(1) Graduation from a medical school of the United States or Canada recognized by the Council on Medical Education and Hospitals of the American Medical Association.

(2) Completion of an internship of not less than one year in a hospital approved by the same council.

(3) In the case of an applicant whose training has been received outside of the United States and Canada, his credentials must be satisfactory to the Advisory Board for Medical Specialties and the Council on Medical Education and Hospitals of the American Medical Association.

Special Training

(1) Five years must elapse after completion of a year's internship in a hospital approved for intern training before the candidate is eligible for examination.

(2) Three years of this period must be devoted to special training in internal medicine. This requirement should include a period of at least several months of graduate work under proper supervision in anatomy, physiology, biochemistry, pathology, bacteriology, or pharmacology, particularly as related to the practice of internal medicine.

This work may be carried on in any domestic or foreign medical school or laboratory recognized by the Council on Medical Education and Hospitals of the American Medical Association as offering appropriate facilities for this type of postgraduate experience; or it may include a period of at least several months of graduate work under proper supervision in internal medicine or in its restricted and specialized branches in any domestic or foreign hospital, clinic, or dispensary, recognized by the above Council as offering appropriate facilities for this type of postgraduate experience.

(3) A period of not less than two years of special practice in the field of internal medicine or in its more restricted and specialized branches.

The American Board of Internal Medicine does not propose to establish fixed rules for the preliminary training of candidates for certification in this field. Broad general principles for training, however, may be outlined, although such suggestions as are made must, of necessity, be subject to constant changes reflecting the dynamic nature of the specialty.

A sound knowledge of physiology ,biochemistry, pharmacology, anâtomy, bacteriology, and pathology, in so far as they apply to disease, is regarded as essential for continued progress of the individual who practices internal medicine. The more factual knowledge of medicine and its basic sciences is not sufficient. The candidate must have had training in their use in furthering his understanding of clinical medicine. This implies practical experience under the guidance of older men who bring to their clinical problems ripe knowledge and critical judgment. Preparation to meet this requirement adequately may

be even more difficult to obtain than the so called scientific training. It may, however, be acquired in the following ways:

(*a*) By work in a well organized hospital outdoor clinic conducted by competent physicians.

(*b*) By a prolonged period of resident hospital appointments likewise directed by skilled physicians.

(*c*) By a period of training in intimate association with a well trained and critical physician who has taken the trouble to teach and guide his assistant rather than to require him only to carry out the minor drudgery of a busy practice.

(4) The Board does not consider it to the best interests of internal medicine in this country that rigid rules as to where or how the training outlined above is to be obtained. Medical teaching and knowledge are international. The opportunities of all prospective candidates are not the same. Some may have the opportunity of widening their knowledge by a period of study abroad. Others, at the other extreme, may be restricted to a comparatively narrow geographic area and their detailed training must be obtained in short periods scattered over a long time. Although it is laid down that at least five years must elapse between the termination of the first intern year and the time when the candidate is eligible to take the examination, a longer period is advisable. The Board wishes to emphasize that the time and training are but means to the end of acquiring a broadness and depth of knowledge of internal medicine which the candidate must demonstrate to the Board in order to justify it in certifying that he is competent to practice internal medicine as a specialty. The responsibility of acquiring the knowledge as best he may rests with the candidate, while the responsibility of maintaining the standard of knowledge required for certification devolves on the Board.

Method of Examination

The examination required of candidates for certification as specialists in Internal Medicine will comprise Part I (written), and Part II (practical or clinical).

PART I. The written examination is to be held simultaneously in different sections of the United States and Canada and will include:

(*a*) Questions in applied physiology, physiologic chemistry, pathology, pharmacology, and the cultural aspects of medicine.

(*b*) Questions in general internal medicine.

The first written examination will be held in December, 1936, and candidates successful in this written test will be eligible for the first practical or clinical examination which will be conducted by members of the Board near the time for the annual session of the American College of Physicians at St. Louis in April, 1937. The second practical examination will be held at Philadelphia near the time of the annual session of the American Medical Association in Atlantic City in June, 1937.

The fee for examination is forty dollars, which must accompany the application, and an additional fee of ten dollars is required when the certificate is issued.

Application blanks and further information can be obtained by addressing the office of the chairman, Walter L. Bierring, M.D., Suite 1210, 406 Sixth Avenue, Des Moines, Iowa, U. S. A.

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